IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Wayne O. Duescher	Examiner:	Lazorcik, Jason L.
Serial No.	10/824,107	Group Art Unit:	3724
Filed:	April 14, 2004	Docket No.:	638.014US1
Title:	ABRASIVE AGGLOMERATE RAISED ISLAND ARTICLES		

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
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The following documents are hereby submitted:

☒ Communication Re.: Submission of Non-Patent References to the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office
☒ Copies of 8 non-patent references
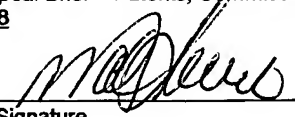☒ Transmittal Sheet
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By: _____
Atty: Mark A. Litman
Reg. No. 26,390

CERTIFICATE UNDER 37 C.F.R. 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described herein, are being deposited in the United States Postal Service, as first class mail, with sufficient postage, in an envelope addressed to: Mail Stop Appeal Brief – Patents, Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on___6 February 2008

Mark A. Litman
Name

Signature

THE UNITED STATES PATENT AND TRADEMARK OFFICE

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COMMUNICATION RE: NON-PATENT REFERENCES

MAIL STOP APPEAL BRIEF
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P.O. Box 1450
Alexandria, VA 22313-1450

Please find enclosed 8 Non-Patent references. The examiner requests that the attorney of record forward the following references to The Board of Patent Appeals and Interferences of the United States Patent and Trademark Office:

- "Simulatios of Sol Gel Materials," Gelb Research Group at Washington University in St. Louis, http://www.chemistry.wustle.edu/~gelb/solgel.html. (later version)

- "Simulatios of Sol Gel Materials" Gelb Research Group at Washington University in ST. Louis, http://www.chemistry.wustle.edu/~gelb/solgel.html. (newer version)

- Stephen Sternowsky, et al., "Experiemental Study and Neural Network Modeling of the Ligament Disintegration in Rotary Atomization," Atomization and Sprays, vol 12, pp 107-121, 2002

- "Silica Aerogels," Ernest Orlando Lawrence Berkely National Laboratory, http://eande.lbl.gov/ECS/aerogels/satoc.htm

- "Silica Aerogels," Microstructures Materials Group, http://eetd.lbl.gov/ECS/aerogels/sa-making.html

- "Introduction to Hybrid Organic-Inorganic Materials (12h), University of Bordeaux-1/Doctoral School of Chemical Sciences PhD students, http:www.icmcb.u-bordeaux.fr/duguet/ostdea.htm

- J. B. Calver, "Colloids," http://mysite.du.edu/~jcalvert/phys/colloid.htm, December 5, 2002.

- Malcolm Summers, et al., "Granulation," Dosage Form Design and Manufacture, pp 364-378

The Examiner is invited to contact Applicant's Representatives, at the below-listed telephone number, if any further changes need to be made to the enclosed drawings. Authorization is hereby given to charge any fees that are owed for the submission of these drawings to Deposit Account Number 50-1391.

Respectfully submitted,

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By His Representatives,

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Date: 6 February 2008   By _____
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Mark A. Litman
Name   Signature

Gelb Research Group at Washington University in St. Louis

Simulations of Sol Gel Materials

(The following material is a brief summary of the project description from our NSF grant "Multi simulations of sol-gel materials." - LDG)

Introduction

Silica xerogels are candidate materials for chemical sensors [1,2,3,4,5,6], drug-delivery syst and novel optical [8,9,10,11] and electrochromic[12,13] applications. They are ubiquitous in chromatography [14,15,16] and catalysis [17,18,19], and are widely used in studies of gas separations [20,21] and as a support matrix for nanocluster research [22,23,19].

Aerogels are very high-porosity materials [24,25,26] used in particle detectors and as therma insulation [27,26], in space probes (for comet-tail dust collection [28]), and in many studies of confined in random media, especially helium and helium mixtures[29,30].

Silica xerogels and aerogels prepared with titanium[31,32], vanadium[33,34,35], or other meta dopants [36], or prepared from other oxides entirely[37,38,17,11,39], are promising materials catalysts and catalyst supports[17,40,41,42] and in electrochemical applications [38,43] and s cells [12,44].

Thin films of xerogels can be prepared by a variety of processes, including spin-coating and coating [45]. Thin films are used in sensors, electronics, optics, lubrication, and other areas.

Templated materials arrived in 1992 with the first preparation of "MCM-41" [46], demonstrat highly regular pore structures could be achieved on scales much larger than those present in Recent developments in templating [47,48,49,50,51,52,53,54] and other micro-patterning technologies[55] suggest the *rational design* of porous media for different applications [56,54] variety of microstructures have now been prepared, including arrays of simple geometries, bicontinuous networks, and hierarchical structures [54,57].

More information on sol-gel stuff in general can be found at:

- The Sol-Gel Gateway
- A Sol Gel Technology site.

Simulations of gel processing

Simulation models, unlike experimental systems, can be quickly and easily characteriz many methods. In a computational study, the systematic optimization of synthesis conditions as temperature and pH to achieve a desired structure is much less time-consuming than in th world. Simulations also clearly reveal *why* and *how* particular structures appear. Thus, the de: cycle would be greatly accelerated by incorporating the predictive capacity of realistic comput modeling.

We are taking a multi-scale approach in this work, using conventional molecular simulation at up to tens of nanometers and a coarse-grained particulate model at mesoscopic scales up to hundred nanometers.

The preparation and properties of xerogels[58,59] and aerogels [27,26] have been compreher reviewed. These materials are prepared through sol-gel processing, in which precursor solutic undergo *gelation*, *aging* and *drying*. Xerogels are prepared by drying at subcritical solvent cor Liquid-vapor interfaces develop in the drying gel, and forces due to surface tension cause sut
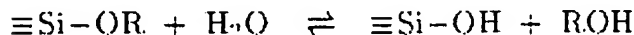
collapse of the gel structure as liquid is removed. Aerogels are dried under *supercritical* (or other [60]) conditions, leading to dry gels with porosity as high as 99.9%. *Consolidation*, or heating at high temperatures, is used to generate densified, non-porous materials for optics and other applications.
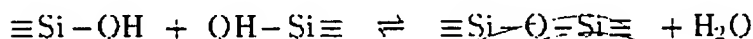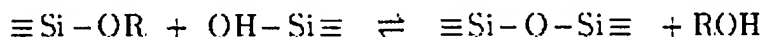
Simulating the preparation of xerogels and aerogels involves separate treatment of gelation, aging, drying, and for non-porous materials, consolidation.

Gelation

In the gelation step, alkoxide gel precursors in aqueous solution are hydrolyzed,

$$\equiv Si - OR + H_2O \rightleftharpoons \equiv Si - OH + ROH$$

and polymerize through alcohol or water producing condensations:

$$\equiv Si - OR + OH - Si \equiv \rightleftharpoons \equiv Si - O - Si \equiv + ROH$$
$$\equiv Si - OH + OH - Si \equiv \rightleftharpoons \equiv Si - O - Si \equiv + H_2O$$

The gel morphology is influenced by temperature, the concentrations of each species (attention focuses on *r*, the water/alkoxide molar ratio, typically between 1 and 50), and especially acidity:

- Acid catalysis generally produces weakly-crosslinked gels which easily compact under drying conditions, yielding low-porosity microporous (smaller than 2 nm) xerogel structures (Figure 3a).

- Conditions of neutral to basic pH result in relatively mesoporous xerogels after drying, as rigid clusters a few nanometers across pack to form mesopores. The clusters themselves may be microporous.

- Under some conditions, base-catalyzed and two-step acid-base catalyzed gels (initial polymerization under acidic conditions and further gelation under basic conditions [61,59]) exhibit *hierarchical* structure and complex network topology (Figure 3c).

The initial stages of gelation, when the average cluster size is very small, are best modeled with a purely atomistic approach. Considerable effort has already gone into developing potential models for this, with convincing results [62,63,64,65,66,67,68].

Hierarchically structured gels and low-density gels cannot be directly treated with molecular models; a meso-scale approach must be used in this case. Relatively dense gels can be modeled with *either* atomistic simulations or coarse-grained simulations.

(a) Acid catalysis

Wet gel (schematic)   xerogel (schematic)   TEM (bar=25nm)
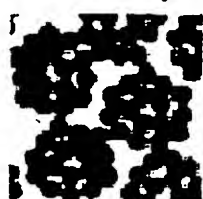
(b) Base catalysis

Wet gel (schematic)   xerogel (schematic)   TEM (bar=100nm)
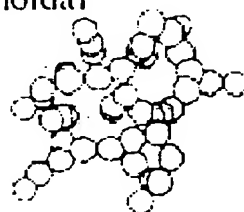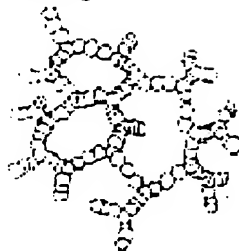
(c) Base–catalyzed colloidal

hierarchical   random packing   TEM (bar=100nm)

(d) Aerogel
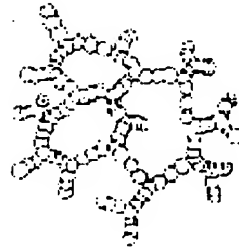
Wet gel (schematic)   dried gel (schematic)   TEM (bar=50nm)

Schematic wet and dry gel morphologies and representative transmission electron micrographs. (Adapted from Brinker and Scherer, Sol Gel Science, chapter 9, figures 3a-3d. [58].)

Aging

Gel aging is an extension of the gelation step in which the gel network is reinforced through further polymerization, possibly at different temperature and solvent conditions. *Syneresis*, the expulsion of solvent due to gel matrix shrinkage, can occur during gel aging.

Simulating aging requires the use of an approach which can access long time scales. The "activation-relaxation technique" (ART) [69,70,71] is being implemented for this purpose. In this method the system is repeatedly moved onto saddle-points in the potential energy hypersurface (e.g., "activation") and then relaxed, efficiently sampling many potential minima. These methods have been successfully applied to amorphous silica [70,71] and can be implemented as an extension of a molecular dynamics code. The relaxation step can be accomplished either by numerical optimization or with molecular dynamics.

Drying

The gel drying process consists of removal of water from the gel system, with simultaneous collapse of the gel structure, under conditions of constant temperature, pressure, and humidity.

In the coarse-grained model (below) the equation of state is trivially calculable, and drying is easily modeled by choosing the solvent chemical potential to favor the vapor phase and allowing the particle positions and cell volume to slowly relax under the influence of solvent capillary forces.

At the molecular scale, we can model this process using an extension of the "Gibbs Ensemble Monte Carlo" technique for binary mixtures [72,73,74], where the mixture consists of water and atmosphere. The atmosphere will be modeled as a single-component gas. In this technique, *two* simulation cells are coupled by mass-exchange moves, in which molecules in one cell are transferred into the other cell. The volumes of the cells fluctuate independently, allowing specification of the pressure. To model constant *humidity*, the water content in the "atmosphere" cell will be controlled by periodic removal of water molecules from the simulation. This is analogous to using dehumidification in an experimental setup, and has the added benefit of requiring only a relatively small "atmosphere" cell.

Consolidation

Xerogels are higher in free energy than conventional amorphous silica (glass) and crystalline silica, as they have a substantial internal surface area and associated surface tension. During heating to temperatures above at least 700 C, the dry gel shrinks substantially and becomes similar to a melt-prepared glass. Many such sintering experiments are done at constant heating rate, which hastens the densification [59,58]. Simulations of consolidation will use molecular models. Both isothermal conditions and constant heating rates can be accessed with standard molecular dynamics simulations and ART as above.

Aerogels

Aerogels can be simulated using the same basic techniques as xerogels, except that the conditions during drying must be chosen above the critical point of the water model. Aerogel systems do not collapse (much) under drying conditions, and supercritical gel drying will be easier to simulate than the subcritical process. High-porosity aerogels are only accessible via the meso-scale model.

Thin films

Experimental studies involving sol-gel *nanocoating* have been reviewed recently by Caruso and Antonietti[54]. The deposition of a gel of several nanometers' thickness upon a surface or nanoparticle allows one to generate novel nanostructured silica materials (via templating, below), or to modify the surface properties of the system. Simulating such processes requires the introduction of the surface or nanoparticle into the simulation cell and suitable intermolecular potentials. For deposition on planar surfaces, as in spin-coating, the concentration of the sol increases as the solvent

evaporates, which can be accounted for using the drying methodology discussed above.

Templated materials

When a gel is formed around a template which is then removed, the process is known as *casting*, and is the most commonly used templating strategy. One may apply casting *twice*, generating a final material with the same structure as the original template; this is reminiscent of the "lost-wax" method of bronze casting[75]. For gelation around a template, suitable models for the template must be introduced.

Our exploratory simulations in this area will focus on two systems with stiff and soft templates, respectively: rigid nanotubes [76], which are easily modeled for these purposes, and the quaternary ammonium surfactants used in preparation of MCM-41 [46], parameterized using the AMBER force field [77].

Meso-scale particulate model and simulations

We are investigating a coarse-grained model for sol-gel materials which replaces each cluster with a single "gel particle", while accounting for size variation of clusters, aggregation through condensation reactions, and solvent effects. The particle-particle interaction will be relatively short-ranged and of a shifted-center Lennard-Jones type, this approximates particle-particle interactions by the van der Waals interactions between atoms *on their surfaces*. Particles may also form bonds upon contact, which are described with Morse-type potentials. Particle sizes of 1-3 nm are appropriate.

The development of a solvent model suitable for drying simulations is not trivial, and will be a major methodological contribution of the proposed work. The solvent in the coarse-grained approach must (a) possesses a liquid-vapor phase diagram and reasonable interfacial properties, (b) be computationally inexpensive to solve, and (c) be sufficiently general that solvent properties and solvent-gel interactions can be fit to molecular simulation results. **These requirements can be met with a lattice-gas model solved in the mean field approximation[78].** The fluid-fluid and fluid-gel interactions will be chosen to mimic atomistic potentials, truncated at a few grid spacings, and parameterized as necessary. Solvent-particle interactions are pairwise-additive, and within the mean-field approximation are simply given by a summation over forces exerted from lattice points within range of a given particle, weighted by the mean-field solution of the densities at those points. In drying simulations, constant pressure can be modeled with volume-change moves in which the simulation cell expands or contracts by one or more lattice spacings.

In strongly inhomogeneous systems, large parts of the simulation cell will be filled with bulk-like water or water vapor. These lattice points can be simply fixed at the appropriate equilibrium densities. This will substantially speed up solution of the model. Specifically, only lattice points within some threshold distance of a gel particle will be considered "active". As long as the pressure is either above condensation or substantially below it, this distance can be as small as several nanometers. The use of more sophisticated multi-scale "multigrid" techniques [79] to improve the performance of the model will be investigated and applied if possible.

Integration of molecular and meso-scale models

Integration of these two approaches requires two types of "translation". The first is the use of the small-scale model to parameterize the large-scale one. [The molecular model parameters could be determined, in principle, *ab initio*, which would introduce a third, subatomic, scale!] The second type of translation moves in the other direction - once the meso-scale model has been used to generate a structure, how can an

atomic-scale description of (part of) that structure be regenerated? This fine-graining is necessary for simulations of molecular-scale processes occurring within a mesoscopic system.

Dense xerogels, which can be treated with both types of simulation, will be used to parameterize the meso-scale model. The initial stages of gelation in the molecular model can be analyzed to create an ensemble of gel particles by tabulation of the size distribution and dispersion of bonding sites. Simulations of the meso-scale model can then be initiated, and its parameters adjusted to obtain agreement of the global structural properties described above.

To reverse the process, one must replace a collection of gel particles with atomistically modeled silica. This is a non-trivial task, since it requires *adding* atomic-scale information to the system, rather than removing it. Two strategies will be employed. In the first, the particle configuration will be used as a template for ``carving'' the atomistic model from a block of amorphous silica, modeled separately. Such templating schemes have been effectively used for MCM-41 type materials [80], with molecular simulation used to equilibrate the unrelaxed surfaces. In the second approach, an ensemble of molecular clusters can be extracted from molecular simulations and used to replace gel particles in the coarse-grained model, matched according to size and arrangement of bonding sites. This would result in a molecular model where only inter-cluster interactions are unrelaxed; molecular dynamics can then be used to achieve mechanical stability.

Thus, in modeling the synthesis of a hierarchically structured or low-density material, we begin with molecular simulations of the gelation step. When the length-scale of aggregation in this simulation exceeds a threshold fraction of the cell size, the simulation would switch over to a coarse-grained model *with equivalent statistical properties*, in a much larger cell. This would be used for the remainder of gelation, aging, and drying. For characterizations by gas adsorption or surface structural analysis, a molecular model could be regenerated from the final coarse-grained configuration. For small-angle scattering or network analysis, either regenerated molecular models or meso-scale models could be used.

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Simulations of Sol Gel Materials

home

(The following material is a brief summary of the project description from our NSF grant "Multi

people   *simulations of sol-gel materials." - LDG)*

publications

research   **Introduction**

software   **Silica xerogels** are candidate materials for chemical sensors [1,2,3,4,5,6], drug-delivery syst

and novel optical [8,9,10,11] and electrochromic[12,13] applications. They are ubiquitous in

resources   chromatography [14,15,16] and catalysis [17,18,19], and are widely used in studies of gas

facilities   separations [20,21] and as a support matrix for nanocluster research [22,23,19].

course pages   **Aerogels** are very high-porosity materials [24,25,26] used in particle detectors and as therma

positions   insulation [27,26], in space probes (for comet-tail dust collection [28]), and in many studies of

confined in random media, especially helium and helium mixtures[29,30].

contact us

Silica xerogels and aerogels prepared with titanium[31,32], vanadium[33,34,35], or other metа
dopants [36], or prepared from other oxides entirely[37,38,17,11,39], are promising materials
catalysts and catalyst supports[17,40,41,42] and in electrochemical applications [38,43] and s
cells [12,44].

Thin films of xerogels can be prepared by a variety of processes, including spin-coating and
coating [45]. Thin films are used in sensors, electronics, optics, lubrication, and other areas.

Templated materials arrived in 1992 with the first preparation of ``MCM-41" [46], demonstrat
highly regular pore structures could be achieved on scales much larger than those present in
Recent developments in templating [47,48,49,50,51,52,53,54] and other micro-patterning
technologies[55] suggest the *rational design* of porous media for different applications [56,54]
variety of microstructures have now been prepared, including arrays of simple geometries,
bicontinuous networks, and hierarchical structures [54,57].

More information on sol-gel stuff in general can be found at:

- The Sol-Gel Gateway
- A Sol Gel Technology site.

Simulations of gel processing
**Simulation models, unlike experimental systems, can be quickly and easily characteriz
many methods.** In a computational study, the systematic optimization of synthesis conditions
as temperature and pH to achieve a desired structure is much less time-consuming than in th
world. Simulations also clearly reveal *why* and *how* particular structures appear. Thus, the *de*
cycle would be greatly accelerated by incorporating the predictive capacity of realistic comput
modeling.

We are taking a multi-scale approach in this work, using conventional molecular simulation at
up to tens of nanometers and a coarse-grained particulate model at mesoscopic scales up to
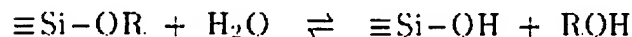hundred nanometers.

The preparation and properties of xerogels[58,59] and aerogels [27,26] have been comprehei
reviewed. These materials are prepared through sol-gel processing, in which precursor solutiс
undergo *gelation, aging* and *drying*. Xerogels are prepared by drying at subcritical solvent соr
Liquid-vapor interfaces develop in the drying gel, and forces due to surface tension cause suг

collapse of the gel structure as liquid is removed. Aerogels are dried under *supercritical* (or ot[[60]) conditions, leading to dry gels with porosity as high as 99.9%. *Consolidation*, or heating ; high temperatures, is used to generate densified, non-porous materials for optics and other applications.
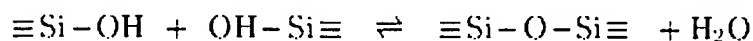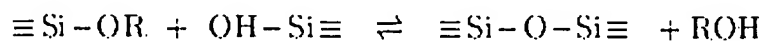
Simulating the preparation of xerogels and aerogels involves separate treatment of gelation, a drying, and for non-porous materials, consolidation.

Gelation

In the gelation step, alkoxide gel precursors in aqueous solution are hydrolyzed,

$$\equiv Si-OR + H_2O \rightleftharpoons \equiv Si-OH + ROH$$

and polymerize through alcohol or water producing condensations:

$$\equiv Si-OR + OH-Si\equiv \rightleftharpoons \equiv Si-O-Si\equiv + ROH$$
$$\equiv Si-OH + OH-Si\equiv \rightleftharpoons \equiv Si-O-Si\equiv + H_2O$$

The gel morphology is influenced by temperature, the concentrations of each species (attentic focuses on *r*, the water/alkoxide molar ratio, typically between 1 and 50), and especially acidit

- Acid catalysis generally produces weakly-crosslinked gels which easily compact under drying conditions, yielding low-porosity microporous (smaller than 2 nm) xerogel structu (Figure 3a).

- Conditions of neutral to basic pH result in relatively mesoporous xerogels after drying, ; rigid clusters a few nanometers across pack to form mesopores. The clusters themselv may be microporous.

- Under some conditions, base-catalyzed and two-step acid-base catalyzed gels (initial polymerization under acidic conditions and further gelation under basic conditions [61,£ exhibit *hierarchical* structure and complex network topology (Figure 3c).
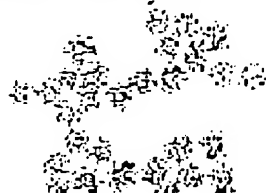
The initial stages of gelation, when the average cluster size is very small, are best modeled w purely atomistic approach. Considerable effort has already gone into developing potential mo for this, with convincing results [62,63,64,65,66,67,68].

Hierarchically structured gels and low-density gels cannot be directly treated with molecular models; a meso-scale approach must be used in this case. Relatively dense gels can be mod with *either* atomistic simulations or coarse-grained simulations.
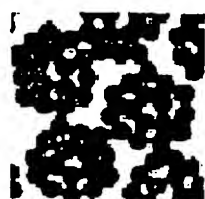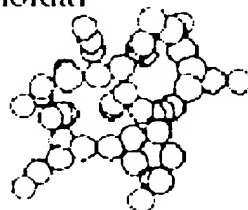
(a) Acid catalysis

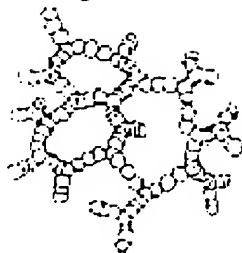Wet gel (schematic)   xerogel (schematic)   TEM (bar=25nm)
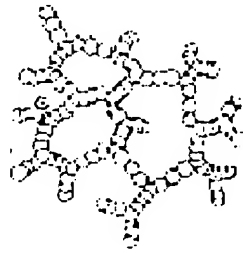
(b) Base catalysis

Wet gel (schematic)   xerogel (schematic)   TEM (bar=100nm)

(c) Base–catalyzed colloidal

hierarchical   random packing   TEM (bar=100nm)

(d) Aerogel

Wet gel (schematic)   dried gel (schematic)   TEM (bar=50nm)

Schematic wet and dry gel morphologies and representative transmission electron micrograph (Adapted from Brinker and Scherer, Sol Gel Science, chapter 9, figures 3a-3d. [58].)

Aging

Gel aging is an extension of the gelation step in which the gel network is reinforced through fu polymerization, possibly at different temperature and solvent conditions. *Syneresis*, the expuls solvent due to gel matrix shrinkage, can occur during gel aging.

Simulating aging requires the use of an approach which can access long time scales. The "activation-relaxation technique" (ART) [69,70,71] is being implemented for this purpose. In tl method the system is repeatedly moved onto saddle-points in the potential energy hypersurfa (e.g., "activation") and then relaxed, efficiently sampling many potential minima. These meth(have been successfully applied to amorphous silica [70,71] and can be implemented as an extension of a molecular dynamics code. The relaxation step can be accomplished either by numerical optimization or with molecular dynamics.

Drying

The gel drying process consists of removal of water from the gel system, with simultaneous collapse of the gel structure, under conditions of constant temperature, pressure, and humidit

In the coarse-grained model (below) the equation of state is trivially calculable, and drying is ε modeled by choosing the solvent chemical potential to favor the vapor phase and allowing the particle positions and cell volume to slowly relax under the influence of solvent capillary force:

At the molecular scale, we can model this process using an extension of the "Gibbs Ensembl Monte Carlo" technique for binary mixtures [72,73,74], where the mixture consists of water an atmosphere. The atmosphere will be modeled as a single-component gas. In this technique, *t* simulation cells are coupled by mass-exchange moves, in which molecules in one cell are transferred into the other cell. The volumes of the cells fluctuate independently, allowing specification of the pressure. To model constant *humidity*, the water content in the "atmosphe cell will be controlled by periodic removal of water molecules from the simulation. This is anal(to using dehumidification in an experimental setup, and has the added benefit of requiring onl relatively small "atmosphere" cell.

Consolidation

Xerogels are higher in free energy than conventional amorphous silica (glass) and crystalline as they have a substantial internal surface area and associated surface tension. During heatir temperatures above at least 700 C, the dry gel shrinks substantially and becomes similar to a prepared glass. Many such sintering experiments are done at constant heating rate, which ha the densification [59,58]. Simulations of consolidation will use molecular models. Both isotheri conditions and constant heating rates can be accessed with standard molecular dynamics simulations and ART as above.

Aerogels

Aerogels can be simulated using the same basic techniques as xerogels, except that the conc during drying must be chosen above the critical point of the water model. Aerogel systems do collapse (much) under drying conditions, and supercritical gel drying will be easier to simulate the subcritical process. High-porosity aerogels are only accessible via the meso-scale model.

Thin films

Experimental studies involving sol-gel *nanocoating* have been reviewed recently by Caruso al Antonietti[54]. The deposition of a gel of several nanometers' thickness upon a surface or nanoparticle allows one to generate novel nanostructured silica materials (via templating, belc to modify the surface properties of the system. Simulating such processes requires the introdt of the surface or nanoparticle into the simulation cell and suitable intermolecular potentials. F(deposition on planar surfaces, as in spin-coating, the concentration of the sol increases as the solvent evaporates, which can be accounted for using the drying methodology discussed abo'

Templated materials

When a gel is formed around a template which is then removed, the process is known as *casi* and is the most commonly used templating strategy. One may apply casting *twice*, generatinc final material with the same structure as the original template; this is reminiscent of the "lost-\

method of bronze casting[75]. For gelation around a template, suitable models for the templat
must be introduced.

Our exploratory simulations in this area will focus on two systems with stiff and soft templates
respectively: rigid nanotubes [76], which are easily modeled for these purposes, and the quat
ammonium surfactants used in preparation of MCM-41 [46], parameterized using the AMBER
field [77].

Meso-scale particulate model and simulations

We are investigating a coarse-grained model for sol-gel materials which replaces each cluste
a single "gel particle", while accounting for size variation of clusters, aggregation through
condensation reactions, and solvent effects. The particle-particle interaction will be relatively s
ranged and of a shifted-center Lennard-Jones type, this approximates particle-particle interac
by the van der Waals interactions between atoms *on their surfaces*. Particles may also form b
upon contact, which are described with Morse-type potentials. Particle sizes of 1-3 nm are
appropriate.

The development of a solvent model suitable for drying simulations is not trivial, and will be a
methodological contribution of the proposed work. The solvent in the coarse-grained approacl
(a) possesses a liquid-vapor phase diagram and reasonable interfacial properties, (b) be
computationally inexpensive to solve, and (c) be sufficiently general that solvent properties an
solvent-gel interactions can be fit to molecular simulation results. **These requirements can b
with a lattice-gas model solved in the mean field approximation**[78]. The fluid-fluid and flt
interactions will be chosen to mimic atomistic potentials, truncated at a few grid spacings, and
parameterized as necessary. Solvent-particle interactions are pairwise-additive, and within the
mean-field approximation are simply given by a summation over forces exerted from lattice pc
within range of a given particle, weighted by the mean-field solution of the densities at those p
In drying simulations, constant pressure can be modeled with volume-change moves in which
simulation cell expands or contracts by one or more lattice spacings.

In strongly inhomogeneous systems, large parts of the simulation cell will be filled with bulk-lik
water or water vapor. These lattice points can be simply fixed at the appropriate equilibrium
densities. This will substantially speed up solution of the model. Specifically, only lattice point:
within some threshold distance of a gel particle will be considered "active". As long as the pre
is either above condensation or substantially below it, this distance can be as small as severa
nanometers. The use of more sophisticated multi-scale "multigrid" techniques [79] to improve
performance of the model will be investigated and applied if possible.

Integration of molecular and meso-scale models

Integration of these two approaches requires two types of "translation". The first is the use of
small-scale model to parameterize the large-scale one. [The molecular model parameters cou
determined, in principle, *ab initio*, which would introduce a third, subatomic, scale!] The secon
of translation moves in the other direction - once the meso-scale model has been used to gen
a structure, how can an atomic-scale description of (part of) that structure be regenerated? Tt
fine-graining is necessary for simulations of molecular-scale processes occurring within a
mesoscopic system.

**Dense xerogels, which can be treated with both types of simulation, will be used to
parameterize the meso-scale model.** The initial stages of gelation in the molecular model cε
analyzed to create an ensemble of gel particles by tabulation of the size distribution and dispε
of bonding sites. Simulations of the meso-scale model can then be initiated, and its paramete·
adjusted to obtain agreement of the global structural properties described above.

To reverse the process, one must replace a collection of gel particles with atomistically model

silica. This is a non-trivial task, since it requires *adding* atomic-scale information to the system rather than removing it. Two strategies will be employed. In the first, the particle configuration be used as a template for ``carving'' the atomistic model from a block of amorphous silica, mo separately. Such templating schemes have been effectively used for MCM-41 type materials | with molecular simulation used to equilibrate the unrelaxed surfaces. In the second approach, ensemble of molecular clusters can be extracted from molecular simulations and used to repl; gel particles in the coarse-grained model, matched according to size and arrangement of bon sites. This would result in a molecular model where only inter-cluster interactions are unrelaxe molecular dynamics can then be used to achieve mechanical stability.

Thus, in modeling the synthesis of a hierarchically structured or low-density material, we begii molecular simulations of the gelation step. When the length-scale of aggregation in this simul; exceeds a threshold fraction of the cell size, the simulation would switch over to a coarse-grai model *with equivalent statistical properties*, in a much larger cell. This would be used for the remainder of gelation, aging, and drying. For characterizations by gas adsorption or surface structural analysis, a molecular model could be regenerated from the final coarse-grained configuration. For small-angle scattering or network analysis, either regenerated molecular m or meso-scale models could be used.

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EXPERIMENTAL STUDY AND NEURAL NETWORK MODELING OF THE LIGAMENT DISINTEGRATION IN ROTARY ATOMIZATION

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An experimental study of the droplet sizes generated by a liquid ligament emerging from a rotary atomizer is described. A high-speed-shutter CCD camera was used to observe the ligament path, the ligament thinning, and the breakup. Droplet sizes were measured with laser diffraction technique. The atomizer consisted of a rotating drum with a small orifice at the lateral surface. Due to the experimental setup, the radial and tangential velocity components of the emerging ligament can be varied independently. The experimental work was carried out with variation of rotational speed, mass flow rate, and fluid composition (mixtures of water, glycerol, and surfactant). A neural network (NN) was applied to model and simulate the droplet diameter for different operating conditions, showing good agreement with the measured values. Based on the NN predictions of the system behavior, the model was used as a tool to detect outliers in the experimental data.

INTRODUCTION

Ligament breakup in rotary atomization is one of the techniques adopted in the industry to produce sprays with narrow size distribution within an acceptable mass flow rate. This method is not commonly used due to the lower mass flow rates that can be achieved in comparison with the lamella disintegration mode. The disadvantage of the lamella disintegration mode is that it generates a larger droplet size distribution. When using conventional rotating disks or cups for atomization, a narrow range of operating conditions, including liquid properties, allows the ligament disintegration mode.

In this study a perforated drum atomizer is used for different fluid compositions, in which a wide range of operating conditions can be used under ligament disintegration mode. The ligament disintegration mode in this case is in many aspects similar to the classical capillary Rayleigh-type jet breakup [1]. The liquid is discharged through a horizontal circular nozzle due to the pressure difference, thus forming a jet, which is then disintegrated into droplets. In order to control the radial and tangential velocity components of the emerging ligament, the liquid mass flow rate can be varied independently of the rotational speed of the drum. This is achieved by controlling the pressure inside the atomizer. Hence, viscous liquids can also be used to form ligaments at suitable mass flow rates. Experiments with a perforated drum were carried out by Piesche [2] without control of

NOMENCLATURE

E	quadratic deviation	W	matrix of weights set in the network
f	sigmoidal function, Eq. (4)	x_i	normalized input variable i in the neural network model
MMD	mass median diameter		
N	number of input variables in the neural network model	X	vector of input signals
NH	number of neurons in the hidden layer	y_k	normalized output variable k in the neural network model
O_j	output from neuron j	ξ	acceleration/damping factor
O_k	output from neuron k in the output layer	φ	rotational angle
p	index of output variables in the neural network model	ω	atomizer angular speed
q	index of input variables in the network		
R^2	coefficient of correlation	**Superscripts**	
r	index of input/output pairs in the learning set		
S	weighted sum of inputs to a neuron	m	point in learning set
v_{rad}	radial velocity of emerging ligament (calculated with mass flow rate)	$'$	first derivative
v_{tan}	tangential velocity of emerging ligament (calculated with rotational speed and outer diameter of the drum)	**Dimensionless Numbers**	
$W_{i,j}$	weight of variable i, in neuron j	Re	Reynolds number (with v_{rad})
		Ro	rotation number ($= v_{tan}/v_{rad}$)

the radial velocity component. He presented a theoretical approach to describe the surface and trajectory of an emerging ligament, showing good agreement with his own experimental data. Corbeels et al. [3] investigated the atomization of various liquids with a high-speed rotary bell atomizer, especially in ligament disintegration mode. They observed that by increasing the rotational speed, smaller droplet sizes are produced, whereas the increase of liquid viscosity at high rotational speeds has no significant effect on droplet size. This fact is explained by the thinning mechanism of the ligament, as a consequence of the divergent motion of adjacent elements of the ligament, as presented by Dombrowski and Lloyd [4].

Liquid properties are of importance for the ligament stretching and breakup. Therefore the viscosity and the surface tension are varied in order to investigate their influences on the breakup length and the resulting particle sizes. In this investigation, the focus is only on Newtonian fluids, avoiding the influence of extensional viscosity.

In order to study the effect of system variables on the size of the droplets produced by the atomizer, a neural network model (NN) was used in fitting the experimental data, thus making use of the ability of such models to simulate the behavior of complex systems based on experimental information.

EXPERIMENTAL

A perforated rotary drum atomizer was built, consisting of a closed hollow cylinder with an orifice located at the lateral surface. In order to study the breakup mechanism of a single ligament, only one orifice was drilled into the atomizer. When in operation, the atomizer

is completely filled with liquid and a capillary jet emerges from the orifice. Due to the rotating movement of the atomizer, the trajectory of the ligament can be described as a spiral. Subsequently, droplets are formed by the Rayleigh-type disintegration process.

The experimental apparatus consists of the rotating perforated drum and the liquid feeding system, including a rotating union and a magnetic inductive flow meter. The mass flow rate is varied between 0.02 and 0.06 liters/min and controlled by a magnetic inductive flow meter. The Reynolds number in the orifice varied between 20 and 4200. The rotational speed can be controlled by an electric motor up to 6000 rpm. The breakup length of the ligament was measured with a triggered CCD camera including a high-speed shutter (JAI M-10, shutter speed down to 2 μs) and is evaluated by image analysis. A trigger mechanism enables the camera to take one picture per rotation of the atomizer. Hence, the influence of various operating conditions can be observed on the computer screen. A Malvern Particle Sizer 2600 with a 1000-mm lens was used to determine the droplet sizes and its distribution by laser diffraction. Repeated measurements showed very good reproducibility in terms of the mass median diamter (MMD), although the level of extinction, which influences the statistical reliability, was low due to the small number of droplets in the measuring volume.

The experimental setup is shown in Fig. 1. The dimensions of the rotary atomizer are as follows: outer diameter of the cylinder 30 mm, orifice diameter 0.37 mm, and orifice length/diameter ratio 2.7.
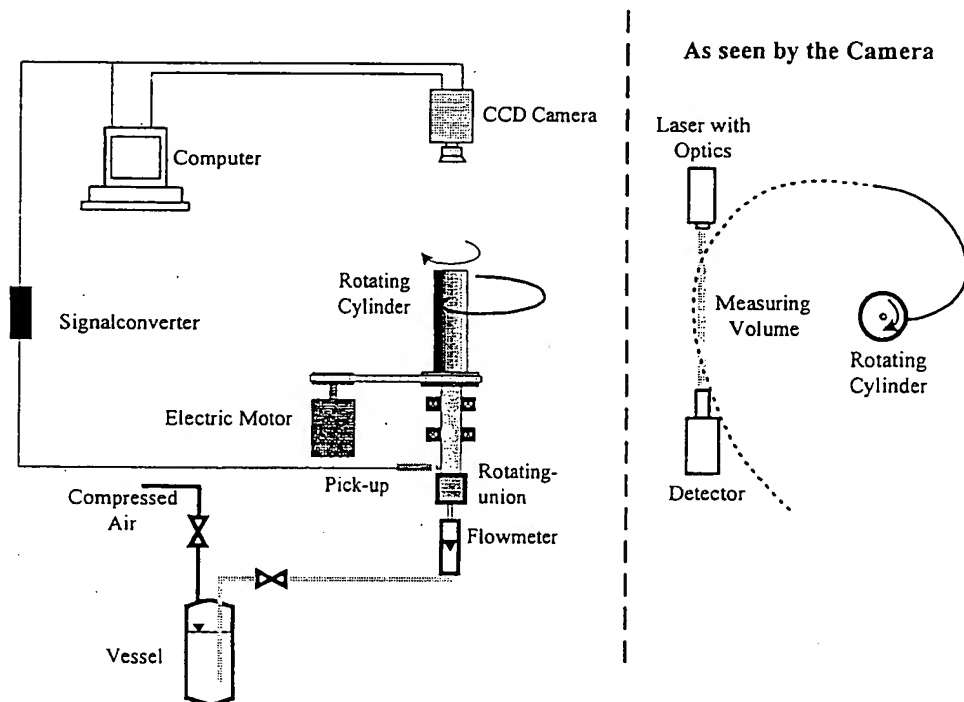
Fig. 1   Schematic of the experimental setup.

Table 1   Liquid Properties at 25°C and Ambient Pressure

Liquid	Density (kg/m³)	Viscosity (mPa · s)	Surface tension (mN/m)
100% water	997	0.9	65.0
55% water + 45% glycerol	1110.2	8.6	51.4
20% water + 80% glycerol	1206.7	53	57.9
10% water + 90% glycerol	1233.0	180	57.7
100% water + surfactant	998.4	0.8	28.8
55% water + 45% glycerol + surfactant	1109.0	5.4	30.9
20% water + 80% glycerol + surfactant	1200.0	40	31.4
10% water + 90% glycerol + surfactant	1226.8	126	31.3

The physical properties of the liquids used in the experiments are given in Table 1. The viscosity was varied by using different mixtures of glycerol and water. Due to the strong relationship between temperature and viscosity, the temperature of the liquid was measured directly before the liquid left the atomizer. The surface tension was changed by adding a surfactant to the liquid, although no previous consideration had been made on its effect on short-time processes such as ligament disintegration.

LIGAMENT BREAKUP AND DROP FORMATION

In Fig. 2a a part of the rotating cylinder and the emerging ligament can be seen (top view), showing the growth of instability waves and the final Rayleigh-type disintegration of the ligament. As the ligament moves away from the orifice, the divergent motion of adjacent elements within the ligament causes stretching (Fig. 2b), which causes a continuous reduction in diameter and consequently smaller droplet sizes at the point of breakup. Hence, the Rayleigh criteria for droplet diameters are not valid in the case of rotating motion of the drum. The stretching process is counteracted by viscous stress and surface tension. The higher viscosity increases the breakup length, promoting the reduction in diameter, leading to smaller droplet sizes. A higher rotation number (Ro = v_{tan} / v_{rad}) caused by higher rotational speed (under constant mass flow rate) leads to a stronger stretching effect of the ligament.

NEURAL NETWORK MODELING

Neural networks (NN) have become a widely used tool in the area of process analysis and simulation. In this work a feed-forward NN with one hidden layer of neurons was used, as illustrated in Fig. 3. Each neuron in the hidden layer (see Fig. 4) first calculates the weighted sum S_j of all interconnected signals from the input layer plus a bias term, Eq. (1), and then generates an output O_j by means of an activation function.

$$S_j = \sum_{i=1}^{N} W_{i,j} \cdot x_j + W_{N+1,j} \qquad (1)$$

(a)   (b)
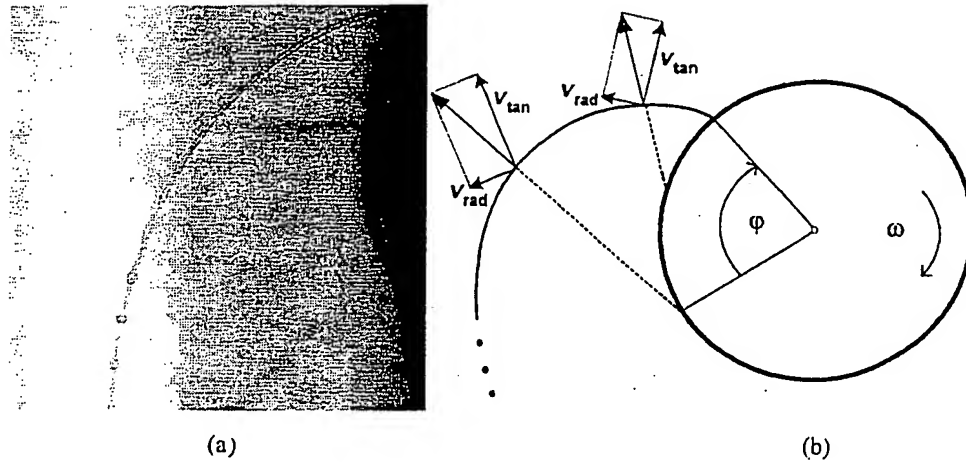
Fig. 2   (*a*) Ligament formation and breakup (seen from above). (*b*) Sketch of ligament path.

One of the most commonly used forms of the activation function is represented by the sigmoidal function, Eq. (2):

$$f(S_{j,k}) = \frac{1}{1+e^{-S_{j,k}}}$$ (2)
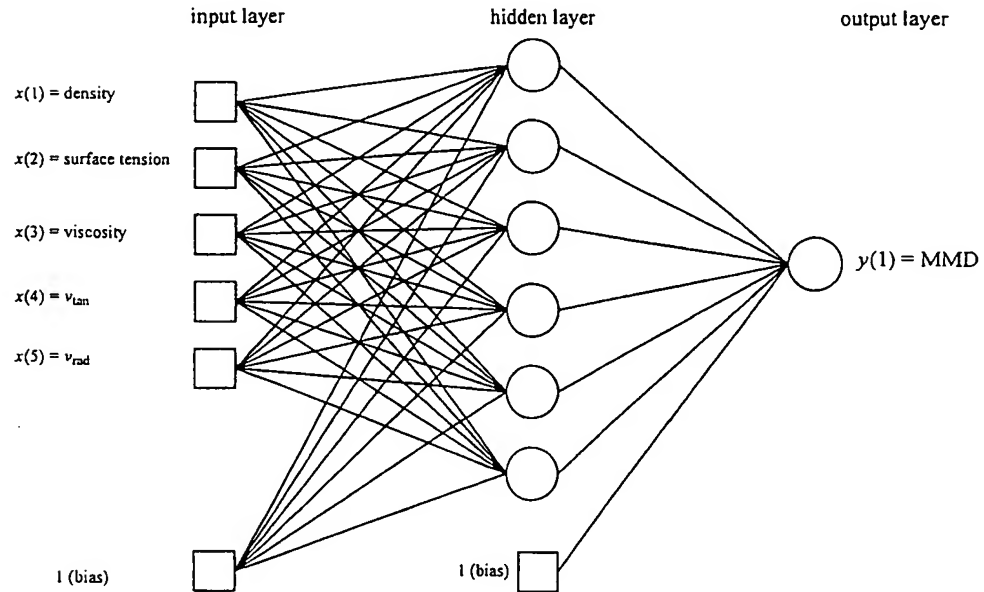
Fig. 3   Structure of the neural network.
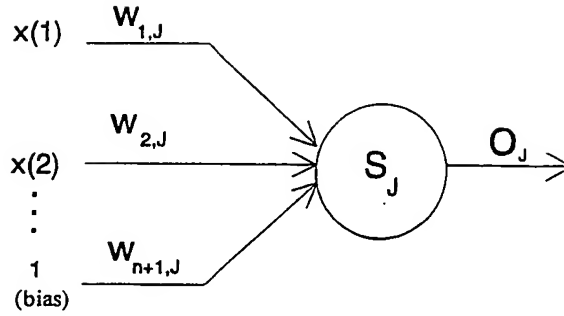
Fig. 4   Illustration of a neuron from the network.

Although other forms of the activation function can be adopted in NN models, the sigmoidal function can be considered as an universal approximator and is able to fit convex and concave multivariable functions [5].

The learning process of a neural network involves making changes in its weights, $W_{i,j}$, so that the quadratic deviation, E, between calculated and experimental values of the output variables, Eq. (3), is minimized.

$$E = \sum_{m=1}^{r}\sum_{k=1}^{p}\left(y_k^{(m)} - O_k^{(m)}\right)^2$$

(3)

where y_k comes from the input–output pairs of data (x, y) available for training the network and O_k, Eq. (4), is the output obtained from Eq. (2) applied to the neurons of the output layer.

$$O_k = f\left(S_k\right)$$

(4)

The most extensively adopted algorithm for the learning phase is the backpropagation, which is a generalization of the steepest descent method [6, 7].

In the traditional gradient approach for minimizing the mean square error with respect to the weights, the derivatives $\delta E/\delta W_{j,k}$ are calculated and the set of weights moves in the direction of steepest descent of the derivative. This technique requires the use of all the input–output pairs to determine the gradient. The backpropagation algorithm also uses gradient information to change the weights. However, they are calculated with respect to only one input–output pair at a time. The weights are updated according to the expressions in Eqs. (5)–(7):

$$W_{j,k}^{(m+1)} = W_{j,k}^{(m)} + \Delta W_{j,k}^{(m)}$$

(5)

for the output layer,

$$\Delta W_{j,k}^{(m)} = \xi \cdot f'(S_k) \cdot \left(y_k^{(m)} - O_k^{(m)} \right) \cdot O_j^{(m)} \tag{6}$$

where ξ represents a damping or accelerating factor. For the hidden layer,

$$\Delta W_{i,j}^{(m)} = \xi \cdot f'(S_j) \left\{ \left[\sum_{k=1}^{p} f'(S_k) \cdot \left(y_k^{(m)} - O_k^{(m)} \right) \cdot W_{j,k}^{(m-1)} \right] X_i^{(m)} \right\} \tag{7}$$

At each iteration the weights between the hidden and output layers are updated first. Subsequently, the weights between the input and hidden layers are changed. After presentation of the first input–output pair, the second pair is processed, and so on.

A number of successful applications of NN models have been developed by the authors in the process industries or in environmental problems, in which no generally accepted or simple phenomenological model can be applied, for instance, computation of particle size distributions from laser diffraction data [8], study of ozone formation in the atmosphere [9], study of the kinetics of photodegradation reactions [10], or the optimization of industrial chemical processes [11].

Since the NN model fitting is essentially a mathematical adaptive regression in which phenomelogical considerations are not used, much care must be taken to validate its representation of the physical process and to prevent overfitting. A simple measure of the quality of the fitting for a given NN is based on comparisons between calculated values and experimental data from the test set (not used in fitting the NN). The use of NN for the purpose of outlier detection was based on the distribution plot of the relative deviations of the median diameter (MMD), as shown in Eq. (8):

$$\text{rel. dev} = \frac{\text{MMD}_{(calc)} - \text{MMD}_{(exp)}}{\text{MMD}_{(exp)}} \tag{8}$$

The computer programs for data preparation, NN fitting, and simulation used in this work were developed at the LSCP–Process Simulation and Control Laboratory, Chemical Engineering Department, University of São Paulo.

RESULTS

For each fluid composition, experiments were performed at different rotational speeds and different mass flow rates. Some representative experimental results are shown in Figs. 5–8, concerning the effect of v_{tan} on MMD, having v_{rad} as parameter, for different glycerol–water mixtures. It can be observed that v_{tan} has a much stronger effect on MMD than v_{rad}, whose effect is clear only when the atomizer is stationary ($v_{tan} = 0$). The effect of the atomizer rotation is less evident at higher rotation speeds (high values of v_{tan}). In the range of experimental

conditions studied, the effect of v_{tan} on MMD becomes more uniform as the amount of glycerol in the mixture increases. No significant effect on MMD was observed by adding surfactant to water, as shown in Fig. 8. From the experimental results shown, no clear tendency can be observed as a consequence of individually changing the process variables, except for v_{tan}. The fitting of a NN model seems to be an adequate tool for studying such tendencies.

The NN fitting was carried out by using about 400 experimental data points (learning set). The validation set contained about 120 data points (test set); these experimental data points are located within the domain of the variables used in the fitting, but are not present in the learning set. Fitting the NN model consisted of varying the number of neurons in the hidden layer (between 4 and 16) and the number of presentations of the set of experimental data points (between 10,000 and 30,000). Figure 9 shows typical behavior of the quadratic deviation, E [Eq. (3)] as a function of the number of presentations of the
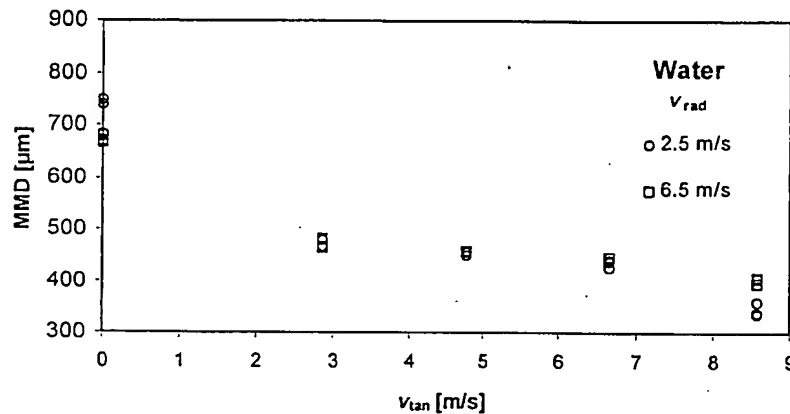
Fig. 5   Experimental results: effect of v_{tan} on MMD, for different values of v_{rad}.
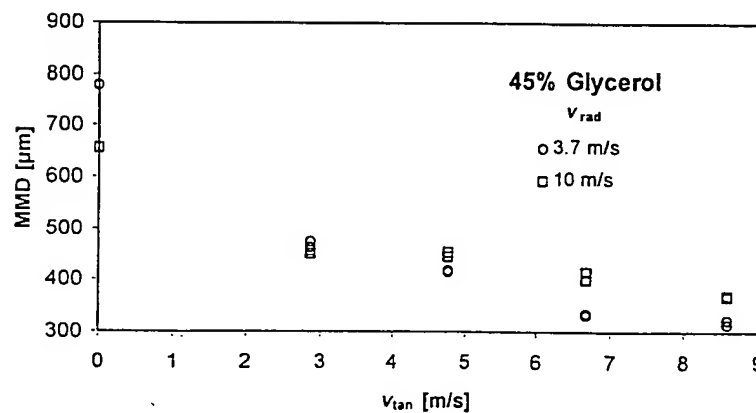
Fig. 6   Experimental results: effect of v_{tan} on MMD, for different values of v_{rad}.
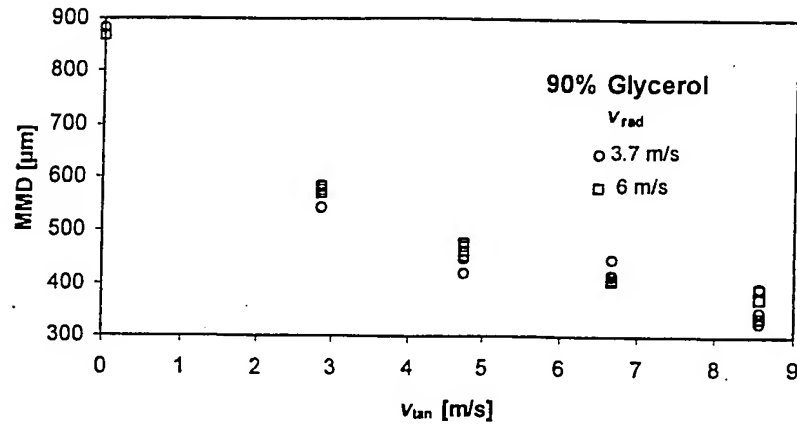
Fig. 7 Experimental results: effect of v_{tan} on MMD, for different values of v_{rad}.
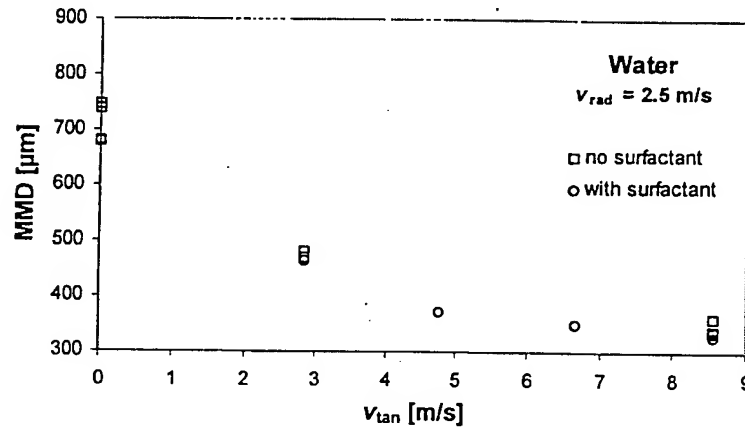
Fig. 8 Experimental results: effect of the surfactant on MMD, for different values of v_{tan}.

data points, for both the learning and test sets. After about 10,000 presentations, no significant decrease in the value of E was observed, indicating that this is an adequate value for this NN fitting parameter. Figure 10 shows comparisons between calculated and experimental values of MMD, for both the learning and test sets, for a NN with 6 neurons in the hidden layer, which resulted in the best fitting obtained. In Fig.11, the relative deviation [Eq. (8)] is shown for data of the test set. For most of these data the relative deviation is smaller than about ±0.15. However, some of the data points showing high values of the relative deviation were further examined by checking the log book of the experiments. It was verified that these points are associated with small problems observed during the experiments (such as orifice clogging, for instance). These points are marked with a different symbol in Fig. 11 and were considered as outliers. They represent a total of 20 points in both learning and test sets. They were taken out from both data sets and the NN fitting
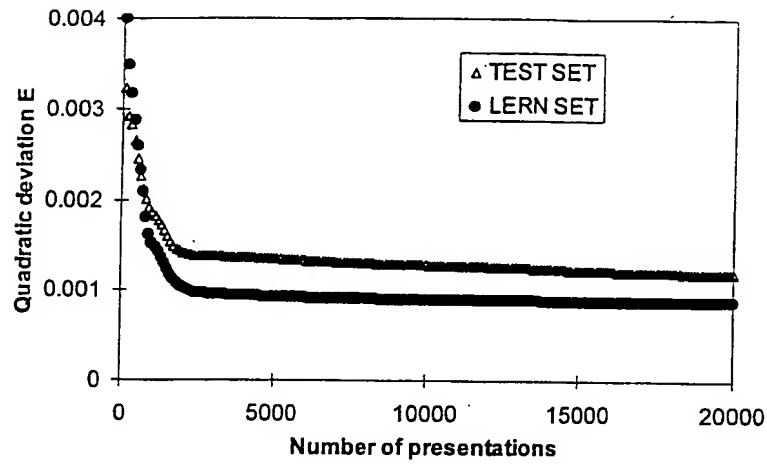
Fig. 9   Quadratic deviation (*E*) as a function of the number of data.
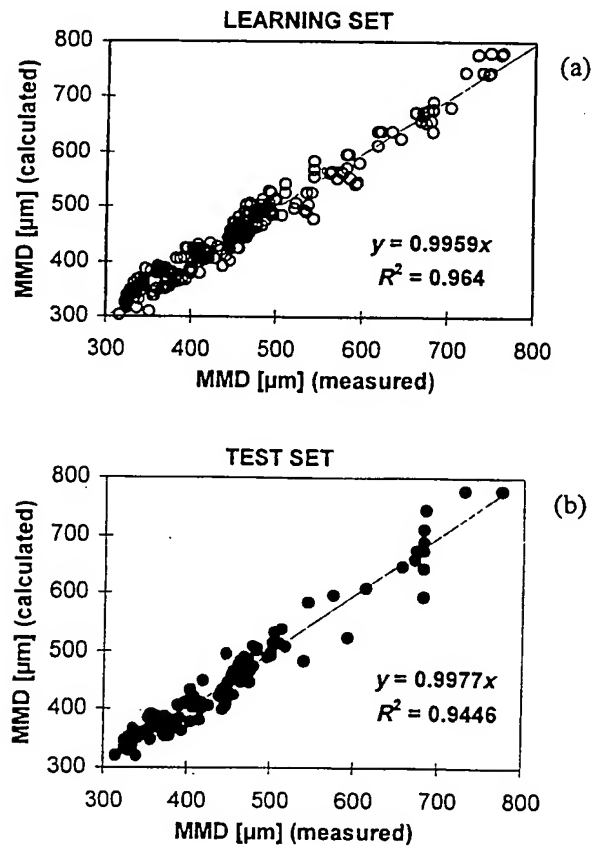
Fig. 10   Comparison of calculated and measured values of MMD (test set and learning set).
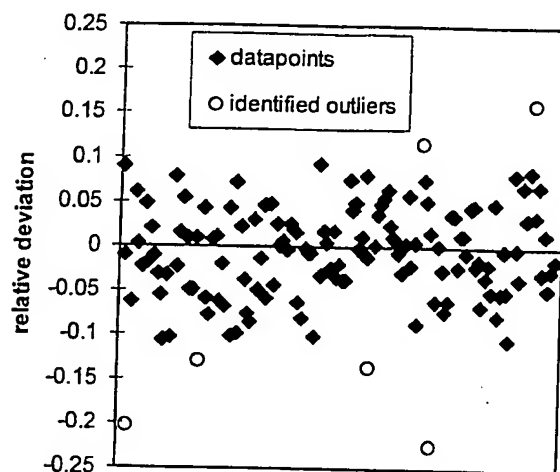
Fig. 11   Relative deviation of calculated MMD values, with identified outliers (test set).
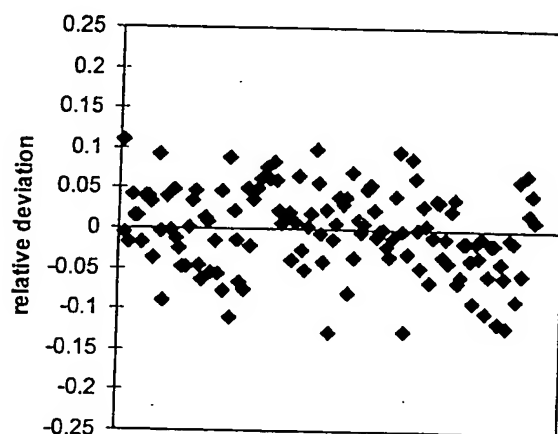
Fig. 12   Relative deviation of MMD values, for the best fitting obtained (test set).

was repeated. The result of eliminating the outliers can be observed in Fig. 12, which shows that the values of the relative deviation for the test set are considerably smaller. Thus, the NN fitting enabled the identification of outliers, whose elimination resulted in a significantly better model fitting. Table 2 presents the weights of the best-fitting NN model for predicting MMD for the rotary drum atomizer studied.

The NN model was then used in a number of simulations, which were carried out in order to study the overall behavior of the system, as well as the effect of individual variables considered. Some of the simulation results are shown in Fig. 13, which presents calculated and experimental values of MMD as a function of v_{tan}, for water with and without surfactant (surface tension 28 mN/m and 65 mN/m, respectively) and at a radial velocity $v_{rad} = 9.5$ m/s.

Table 2 Weights between Input and Hidden Layer and between Hidden and Output Layer, for the Best-Fitting NN Model, Obtained under the Following Conditions: 20,000 Presentations of the Data Set, 6 Neurons in the Hidden Layer, Normalization Range of the Variables 0.1 to 0.9

	Neuron 1	Neuron 2	Neuron 3	Neuron 4	Neuron 5	Neuron 6	Output neuron
Input 1 (density)	2.2785	2.1632	2.5403	−5.7306	−8.0204	−4.7161	−8.1939
Input 2 (surface tension)	1.2616	−0.7564	2.5847	3.632	−2.4939	−1.4855	1.7284
Input 3 (viscosity)	−1.3631	0.2911	2.3261	2.6331	0.45109	0.71096	8.4444
Input 4 (v_{tan})	0.5263	−3.3775	−2.4613	−0.7195	2.5428	16.438	1.0356
Input 5 (v_{rad})	3.0185	0.44871	10.876	−0.1839	−6.163	3.6901	8.8013
Bias	0.97569	0.88388	−0.1811	0.41924	−0.9189	−0.4356	−2.0409
							−0.2816
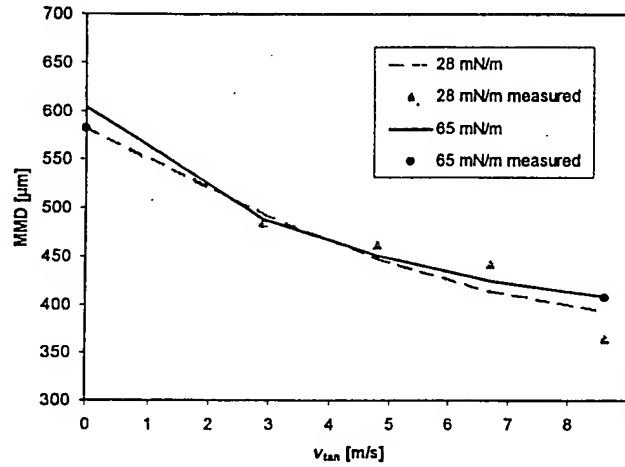
Fig. 13 Comparison of calculated and experimental values of MMD for water at v_{rad} = 9.5 m/s and two different values of surface tension.

It can be observed that the model can simulate the tendency observed in the experimental results, for both variables considered. The overall system behavior in terms of the MMD is shown in Figs. 14 and 15, in terms of response surfaces as a function of v_{tan} and v_{rad}, for water and for the 90% glycerol mixture, respectively. It can be seen that the tangential velocity has the major influence on the median droplet size, whereas the radial velocity has an ambiguous effect on the droplet size. For very low tangential velocities an increase in radial velocity leads to smaller droplet sizes due to the enhanced turbulent action. At high tangential velocities the droplet size increases with higher radial velocity. This is in accordance with the experimental observations. The influence of the fluid composition (amount of glycerol in the mixture) is shown in Fig. 16 in terms of the effect of the tangential velocity on the droplet size, for v_{rad} = 7 m/s and different values of fluid viscosity. It can be noticed that an increase in viscosity from 1 mPa · s to 10 mPa · s leads to smaller droplet sizes. A further increase in viscosity up to 100 mPa · s results in larger droplet sizes compared to those with
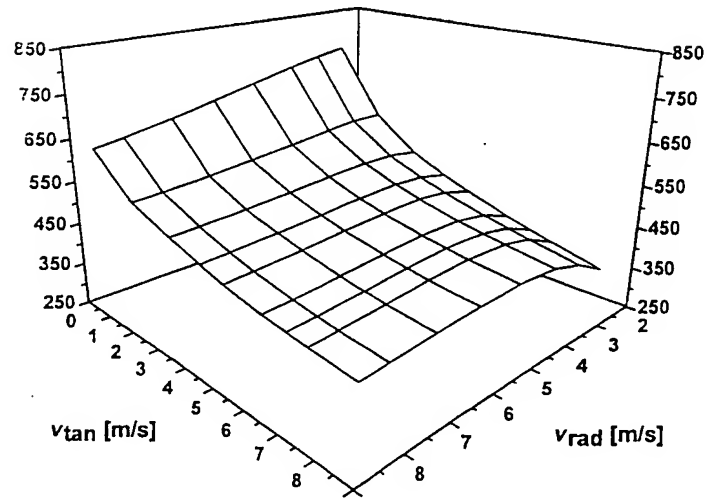
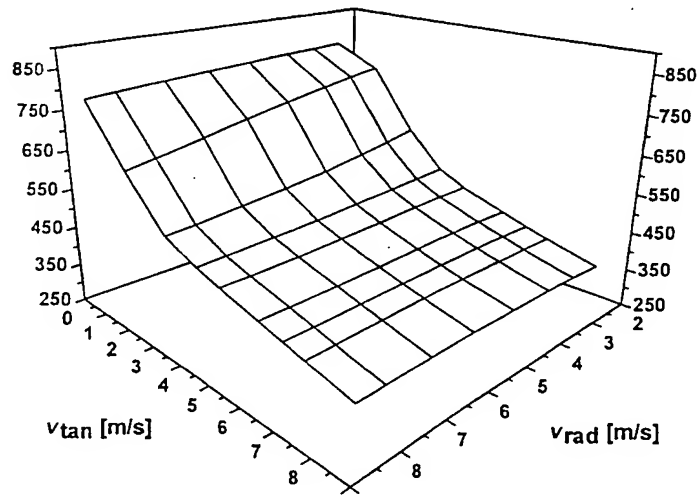Fig. 14 Response level surface of MMD for water.

Fig. 15 Response level surface of MMD for 90% glycerol/10% water.

10-mPa s fluid. The reason for this is the stretching effect of the ligament, already described. However, beyond a certain viscosity level this stretching effect seems to be counteracted by viscous forces and therefore no further reduction in droplet size is achieved.

An evaluation of the relative importance of the NN model variables was done, based on the sum of the absolute values of the weights from the NN input layer, associated to each input variable (larger values of this sum indicate that the variable considered has
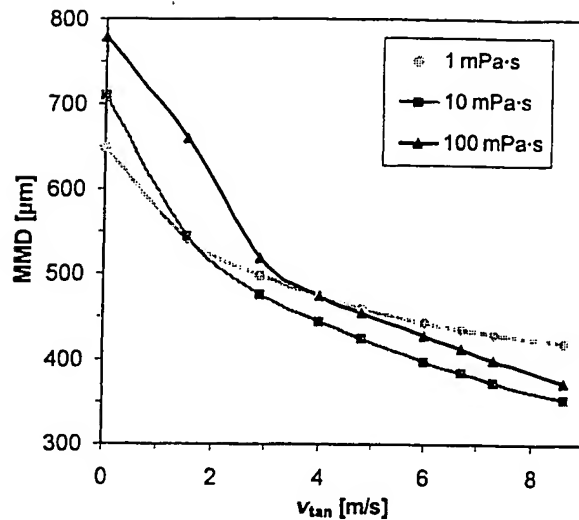
Fig. 16   Influence of liquid viscosity on MMD for v_{rad} = 7 m/s.

higher influence on the model). The largest values of the sum correspond to the tangential velocity and fluid density, followed by the radial velocity, indicating that these three variables have the largest effect on the model. The values of the sum corresponding to the fluid surface tension and viscosity are about one-third of the previous ones, indicating that these two variables have a considerably smaller influence on the model than the other three. Although the properties of the liquid were not varied independently and their influence has not been verified experimentally, these results correspond to the experimental observations described, concerning the behavior of the atomization system studied.

CONCLUSIONS

The rotary drum atomizer operating according to the ligament disintegration mode produces droplets with a narrow size distribution and can operate under different conditions, since the radial and tangential components of the fluid motion can be varied independently. The experimental results aimed at studying the effect of operating variables on the median droplet diameter have shown that the rotational speed (v_{tan}) has the major influence on droplet size, while other variables such as the fluid flow rate (v_{rad}), fluid viscosity, and surface tension appear to have a less pronounced effect.

The use of a neural network model to fit the experimental data enabled the identification of experimental points, which did not follow the overall behavior of the system. After a detailed check of these points, they could be associated with experimental problems and were classified as outliers. Thus, due to the high potential of neural networks to simulate the behavior of complex systems, they can be a powerful tool to identify outliers.

By using a properly trained neural network, simulations were carried out under different conditions, with respect to the MMD. Furthermore, the influence of the process

variables could be studied. The results of the training of the neural network indicate that the adopted modeling approach can be used as a tool to study the behavior of rotary drum atomizers. Further studies are now in the planning stage, in order to obtain a more detailed description of the system, under a wider range of variables.

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ERNEST ORLANDO LAWRENCE BERKELEY NATIONAL LABORATORY

Silica Aerogels

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Note: As of April 02004, this site will no longer be updated. Arlon, after many entered a well-deserved state of semi-retirement. Mike, has also moved on to ot content with its content as it is today. In all honesty, the Light Scattering section since 1995 will probably never come to fruition. The Lab will keep these pages ; but e-mail inquiries may go unanswered. We hope that you have, and will contin

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6, 2004

Back to the Microstructured Materials Group HomePage | Aerogel/Science Questions? | Webmaster

The Learning Kingdom's COOL SITE OF THE DAY

The Sol-Gel Gateway

Solgel Gateway's Site of the month for November 2000!

Microstructured Materials Group

SilicaAeroGels

PHOTO GALLERY   OPPORTUNITIES / AVAILABILITY   PUBLICATIONS   LINKS

MAKING silica aerogels

The discussion below relies upon the following terms:

Hydrolysis:
The reaction of a metal alkoxide (M-OR) with water, forming a metal hydroxide (M-OH).

Condensation:
A condensation reaction occurs when two metal hydroxides (M-OH + HO-M) combine to give a metal oxide species (M-O-M). The reaction forms one water molecule.

Sol:
A solution of various reactants that are undergoing hydrolysis and condensation reactions. The molecular weight of the oxide species produced continuously increases. As these species grow, they may begin to link together in a three-dimensional network.

Gel Point:
The point in time at which the network of linked oxide particles spans the container holding the Sol. At the gel point the Sol becomes an Alcogel.

Alcogel (wet gel):
At the gel point, the mixture forms a rigid substance called an alcogel. The alcogel can be removed from its original container and can stand on its own. An alcogel consists of two parts, a solid part and a liquid part. The solid part is formed by the three-dimensional network of linked oxide particles. The liquid part (the original solvent of the Sol) fills the free space surrounding the solid part. The liquid and solid parts of an alcogel occupy the same apparent volume.

Supercritical fluid:
A substance that is above its critical pressure and critical temperature. A supercritical fluid possesses some properties in common with liquids (density, thermal conductivity) and some in common with gases (fills its container, does not have surface tension).

Aerogel:
What remains when the liquid part of an alcogel is removed without damaging the solid part (most often achieved by supercritical extraction). If made correctly, the aerogel retains the original shape of the alcogel and at least 50% (typically >85%) of the alcogel's volume.
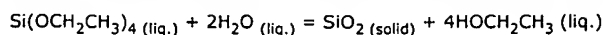
Xerogel:
What remains when the liquid part of an alcogel is removed by evaporation, or similar methods. Xerogels may retain their original shape, but often crack. The shrinkage during drying is often extreme (~90%) for xerogels.

Sol-Gel Chemistry

The formation of aerogels, in general, involves two major steps, the formation of a wet gel, and the drying of the wet gel to form an aerogel. Originally, wet gels were made by the aqueous condensation of sodium silicate, or a similar material. While this process worked well, the reaction formed salts within the gel that needed to be removed by many repetitive washings (a long, laborious procedure). With the rapid development of sol-gel chemistry over the last few decades, the vast majority of silica aerogels prepared today utilize silicon alkoxide precursors. The most common of these are tetramethyl orthosilicate (TMOS, $Si(OCH_3)_4$), and tetraethyl orthosilicate (TEOS, $Si(OCH_2CH_3)_4$). However, many other alkoxides, containing various organic functional groups, can be used to impart different properties to the gel. Alkoxide-based sol-gel chemistry avoids the formation of undesirable salt by-products, and allows a much greater degree of

control over the final product. The balanced chemical equation for the formation of a silica gel from TEOS is:

$$Si(OCH_2CH_3)_4 \text{ (liq.)} + 2H_2O \text{ (liq.)} = SiO_2 \text{ (solid)} + 4HOCH_2CH_3 \text{ (liq.)}$$

The above reaction is typically performed in ethanol, with the final density of the aerogel dependent on the concentration of silicon alkoxide monomers in the solution. Note that the stoichiometry of the reaction requires two moles of water per mole of TEOS. In practice, this amount of water leads to incomplete reaction and weak, cloudy aerogels. Most aerogel recipes, therefore, use a higher water ratio than is required by the balanced equation (anywhere from 4-30 equivalents).

Catalysts

The kinetics of the above reaction are impractically slow at room temperature, often requiring several days to reach completion. For this reason, acid or base catalysts are added to the formulation. The amount and type of catalyst used play key roles in the microstructural, physical and optical properties of the final aerogel product.

Acid catalysts can be any protic acid, such as HCl. Basic catalysis usually uses ammonia, or, more commonly, ¬mmonia and ammonium fluoride. Aerogels prepared with acid catalysts often show more shrinkage during upercritical drying and may be less transparent than base catalyzed aerogels. The microstructural effects of various catalysts are harder to describe accurately, as the substructure of the primary particles of aerogels can be difficult to image with electron microscopy. All show small (2-5 nm diameter) particles that are generally spherical or egg-shaped. With acid catalysis, however, these particles may appear "less solid" (looking something like a ball of string) than those in base-catalyzed gels.

As condensation reactions progress the sol will set into a rigid gel. At this point, the gel is usually removed from its mold. However, the gel must be kept covered by alcohol to prevent evaporation of the liquid contained in the pores of the gel. Evaporation causes severe damage to the gel and will lead to poor quality aerogels

Single-Step vs. Two-Step Aerogels

Typical acid or base catalyzed TEOS gels are often classified as "single-step" gels, referring to the "one-pot" nature of this reaction. A more recently developed approach uses pre-polymerized TEOS as the silica source. Pre-polymerized TEOS is prepared by heating an ethanol solution of TEOS with a sub-stoichiometric amount of water and an acid catalyst. The solvent is removed by distillation, leaving a viscous fluid containing higher molecular weight silicon alkoxy-oxides. This material is redissolved in ethanol and reacted with additional water under basic conditions until gelation occurs. Gels prepared in this way are known as "two-step" acid-base catalyzed gels. Pre-polymerized TEOS is available commercially in the U.S. from Silbond Corp. (Silbond H-5).

These slightly different processing conditions impart subtle, but important changes to the final aerogel product. Single-step base catalyzed aerogels are typically mechanically stronger, but more brittle, than two-step aerogels. While two-step aerogels have a smaller and narrower pore size distribution and are often optically clearer than single-step aerogels.

Aging and Soaking

When a sol reaches the gel point, it is often assumed that the hydrolysis and condensation reactions of the silicon alkoxide reactant are complete. This is far from the case. The gel point simply represents the time when the polymerizing silica species span the container containing the sol. At this point the silica backbone of the gel contains a significant number of unreacted alkoxide groups. In fact, hydrolysis and condensation can continue for several times the time needed for gelation. Failure to realize, and to accommodate this fact is one of the most common mistakes made in preparing silica aerogels. The solution is simple--patience. Sufficient time must be given for the strengthening of the silica network. This can be enhanced by controlling the pH and water content of the covering solution. Common aging procedures for base catalyzed gels typically involve soaking the gel in an alcohol/water mixture of equal proportions to the original sol at a pH of 8-9 (ammonia). The gels are best left undisturbed in this solution for up to 48 hours.

This step, and all subsequent processing steps, are diffusion controlled. That is, transport of material into, and out of, the gel is unaffected by convection or mixing (due to the solid silica network). Diffusion, in turn, is affected by the thickness of the gel. In short, the time required for each processing step increases dramatically as the thickness of the gel increases. This limits the practical production of aerogels to 1-2 cm-thick pieces.

After aging the gel, all water still contained within its pores must be removed prior to drying. This is simply accomplished by soaking the gel in pure alcohol several times until all the water is removed. Again, the length of time required for this process is dependent on the thickness of the gel. Any water left in the gel will not be removed by supercritical drying, and will lead to an opaque, white, and very dense aerogel.

Supercritical Drying

The final, and

most important, process in making silica aerogels is supercritical drying. This is where the liquid within the gel is removed, leaving only the linked silica network. The process can be performed by venting the ethanol above its critical point (high temperature- very dangerous) or by prior

Process conditions for both the carbon dioxide substitution/drying process and the alcohol drying process.

solvent exchange with CO_2 followed by supercritical venting (lower temperatures-less dangerous) It is imperative that this process only be performed in an autoclave specially designed for this purpose (small autoclaves used by electron microscopists to prepare biological samples are acceptable for CO_2 drying). The process is as follows. The alcogels are placed in the autoclave (which has been filled with ethanol). The system is pressurized to at least 750-850 psi with CO_2 and cooled to 5-10 degrees C. Liquid CO_2 is then flushed through the vessel until all the ethanol has been removed from the vessel and from within the gels. When the gels are ethanol-free the vessel is heated to a temperature above the critical temperature of CO_2 (31 degrees C). As the vessel is heated the pressure of the system rises. CO_2 is carefully released to maintain a pressure slightly above the critical pressure of CO_2 (1050 psi). The system is held at these conditions for a short time, followed by the slow, controlled release of CO_2 to ambient pressure. As with previous steps, the length of time required for this process is dependent on the thickness of the gels. The process may last anywhere from 12 hours to 6 days.

At this point the vessel can be opened and the aerogels admired for their intrinsic beauty.

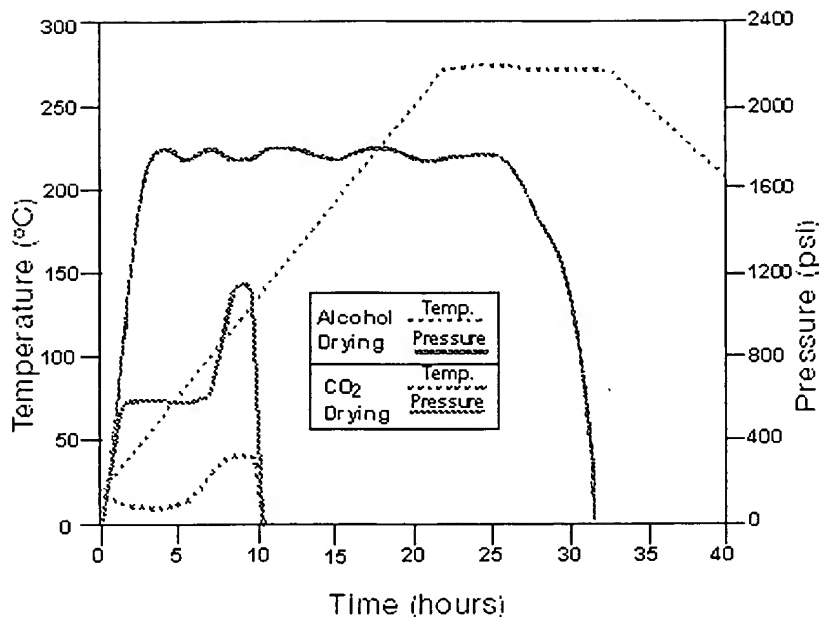## Typical Recipes
Single-Step Base Catalyzed Silica Aerogel
This will produce an aerogel with a density of approx. 0.08 g/cm³. The gel time should be 60-120 minutes, depending on temperature.

1. Mix two solutions:
   a. Silica solution containing 50 mL of TEOS, 40 mL of ethanol
   b. Catalyst solution containing 35 mL of ethanol, 70 mL of water, 0.275 mL of 30% aqueous ammonia, and 1.21 mL of 0.5 M ammonium fluoride.
2. Slowly add the catalyst solution to the silica solution with stirring.
3. Pour the mixture into an appropriate mold until gelation.
4. Process as described above.

Two-Step Acid-Base Catalyzed Silica Aerogel
This will produce an aerogel with a density of approx. 0.08 g/cm³. The gel time should be 30-90 minutes, depending on temperature.

1. Mix two solutions:
   a. Silica solution containing 50 mL of precondensed silica (Silbond H-5, or equivalent), 50mL of ethanol
   b. Catalyst solution containing 35 mL of ethanol, 75 mL of water, and 0.35 mL of 30% aqueous ammonia.
2. Slowly add the catalyst solution to the silica solution with stirring.

3. Pour the mixture into an appropriate mold until gelation.
4. Process as described above.

[ ]

Prof. Etienne Duguet

teaching activity

University of Bordeaux-1 / Doctoral School of Chemical Sciences
PhD students
Introduction to Hybrid Organic-Inorganic Materials (12 h)

objectives ● contents ● timetable ● doctoral school ● university of Bordeaux-1

class objectives

●just an **introduction to HOIM**
●rather from the **polymer chemist point of view**
●**description of the chemical tools** : polymer chemistry, sol-gel process, intercalation chemistry and chemical modification of inorganic surfaces
●description of **HOIM examples** with their versatile properties and main applications

contents

1 - General introduction   OVERHEADS
    1.1 - The HOIM concept
      a) HOIM definition
      b) why such materials ?
    1.2 - Classification attempt
    1.3 - Class objectives
    1.4 - Contents

2 - Macromolecular synthesis background   OVERHEADS
    2.1 - Basic definitions
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      b) homopolymer and copolymer
      c) thermoplastics, elastomers and thermosets
      d) molar mass and degree of polymerization
    2.2 - Classification of polymerization reaction
    2.3 - Step polymerization
      a) polycondensation and polyaddition
      b) molar mass control for linear step polymerization
      c) gelation during non-linear step polymerization
    2.4 - Chain polymerization : free-radical polymerization
      a) initiation, propagation and termination
      b) rate and degree of polymerization
      c) chain transfer reactions
      d) bulk polymerization and its alternative
      e) emulsion polymerization

3 - Sol-gel chemistry and engineering background   OVERHEADS
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    3.2   - Chemical reactivity of metal alkoxides

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b) reactivity of non-silicate tetravalent alkoxides
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b) aging
c) drying (dessication)
d) firing
3.4 - Applications and limitations of sol-gel techniques
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b) drawbacks
c) applications
d) conclusion

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7 - Core-shell hybrid organic-inorganic particles   OVERHEADS
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b) precipitation from soluble precursors in polymer particles
7.2 - Encapsulation processes of inorganic particles
a) surface modification with heterofunctional metal alkoxides
b) adsorption of macromolecules
c) encapsulation through suspension polymerization
d) encapsulation through emulsion polymerization

Last update : 22/01/2007

HOIM = Hybrid Organic-Inorganic Materials acronym

1 – <u>The HOIM concept</u>

   a) HOIM definition

: multiphase material brought about by combining materials that differ in composition or form in order to obtain specific characteristics and properties.

   ➢ retain their identities and properties
   ➢ act in concert to achieve improved synergistic properties

   These traditional composite materials, and in particular materials with I fillers in O matrix, have macroscale domain size of <u>micrometer</u> and even millimeter scale.

        or   or   : a new class of composite materials with the physical constraint of <u>few nanometers</u> as the maximum size of the I and/or O component.

   ➢ I/O interface tends towards infinite.
   ➢ original properties, such as optical transparency.

BUT   I and O components can not be prepared separately before assembling

        ➢ simultaneous syntheses in the same batch
        ➢ successive syntheses

AND   O components are "fragile" (< 250°C)

SO   I component processing and/or modification at temperatures substantially lower than those of conventional ceramic processing conditions :

        ➢
        ➢

b) why such materials ?

When intimately associated

- I component acts as : chemical resistance, mechanical resistance, optical transparency…
- O component acts as or : processability, hydrophobic/hydrophilic balance, specific property as NLO response, biological activity…

➢ synthesis and application of HOIM have attracted

- polymer scientists   and ■ physicists
- solid state chemists   ■ biologists
- ceramists
- inorganic chemists
- organ(ometall)ic chemists

Today the cooperation between them is very important to understand the basic chemistry in conjunction with structure in order to speed up the applications

➢ among present applications of HOIM :

- abrasion resistant coating on plastics
- decorative and functional coating on glasses
- coatings and adhesives for glass fibers
- NLO devices
- contact lenses
- …

2 – <u>Classification attempt</u>

HOIM could be classified according to

- the vol. % of the I (or O) component and the size of the dispersed phase
- dimensional organization types of one component towards the other one

increasing vol. % of I component ↑

ceramics

doped xerogels

decreasing dimensional organization of one component towards the other one →

filled xerogels

| **entangled 3D-networks** | **alternated 2D-layers** | **core-shell particles** |

microcomposites materials

reinforced and/or crosslinked O polymers

O polymers

increasing vol. % of O component ↓
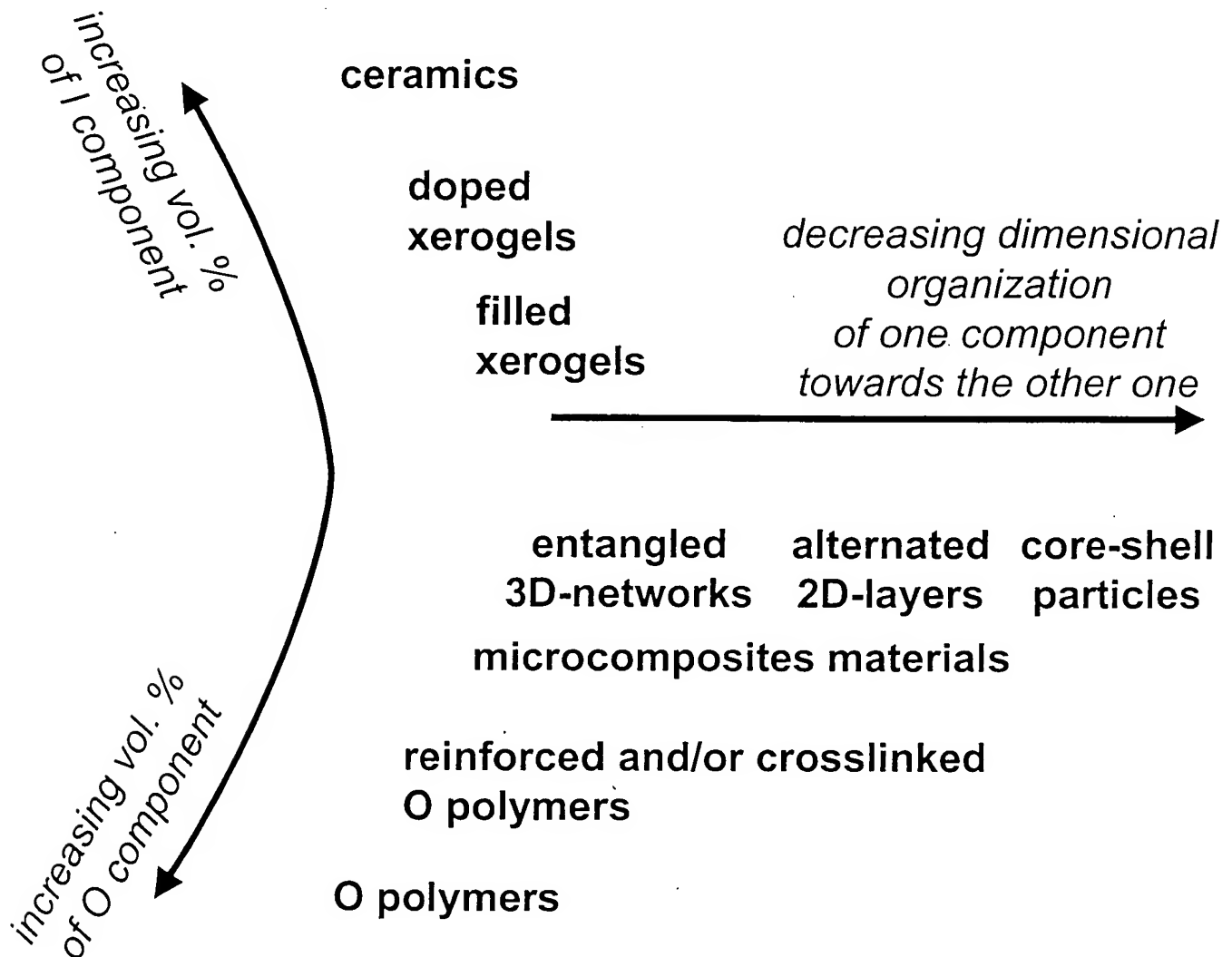
- ➤ simplifying and non-exhaustive classification
- ➤ some of these classes do not fulfil the requirements of nanoscale component size

BUT shared feature : **the controlled association of I and O components through the chemical design of inner interfaces**

3 – Class objectives

➤ just an introduction to HOIM

➤ rather from the polymer chemist point of view

➤ description of the chemical tools :

    ■ polymer chemistry

    ■ sol-gel process

    ■ intercalation chemistry

    ■ chemical modification of I surfaces

➤ HOIM examples with their versatile properties and main applications

4 – Contents

1 ■ General introduction

2 ■ Macromolecular synthesis background

    ◆ Basic definitions

    ◆ Classification of polymerization reactions

    ◆ Step polymerization

    ◆ Chain polymerization : free-radical polymerization

3 ■ Sol-gel chemistry and engineering background

    ◆ General mechanisms in the metal-organic route

    ◆ Chemical reactivity of metal alkoxides

    ◆ Gelation, aging, drying and firing

    ◆ Applications and limitations of sol-gel techniques

4 ■ Sol-gel-derived hybrid organic-inorganic materials

- ◆ Incorporation of small organic molecules or organic groups/functions in inorganic networks
- ◆ Sol-gel process in combination with organic polymers and/or free-radical polymerization reactions
- ◆ Incorporation of micrometric size "objects" in inorganic networks

5 ■ Intercalation chemistry background

- ◆ General considerations
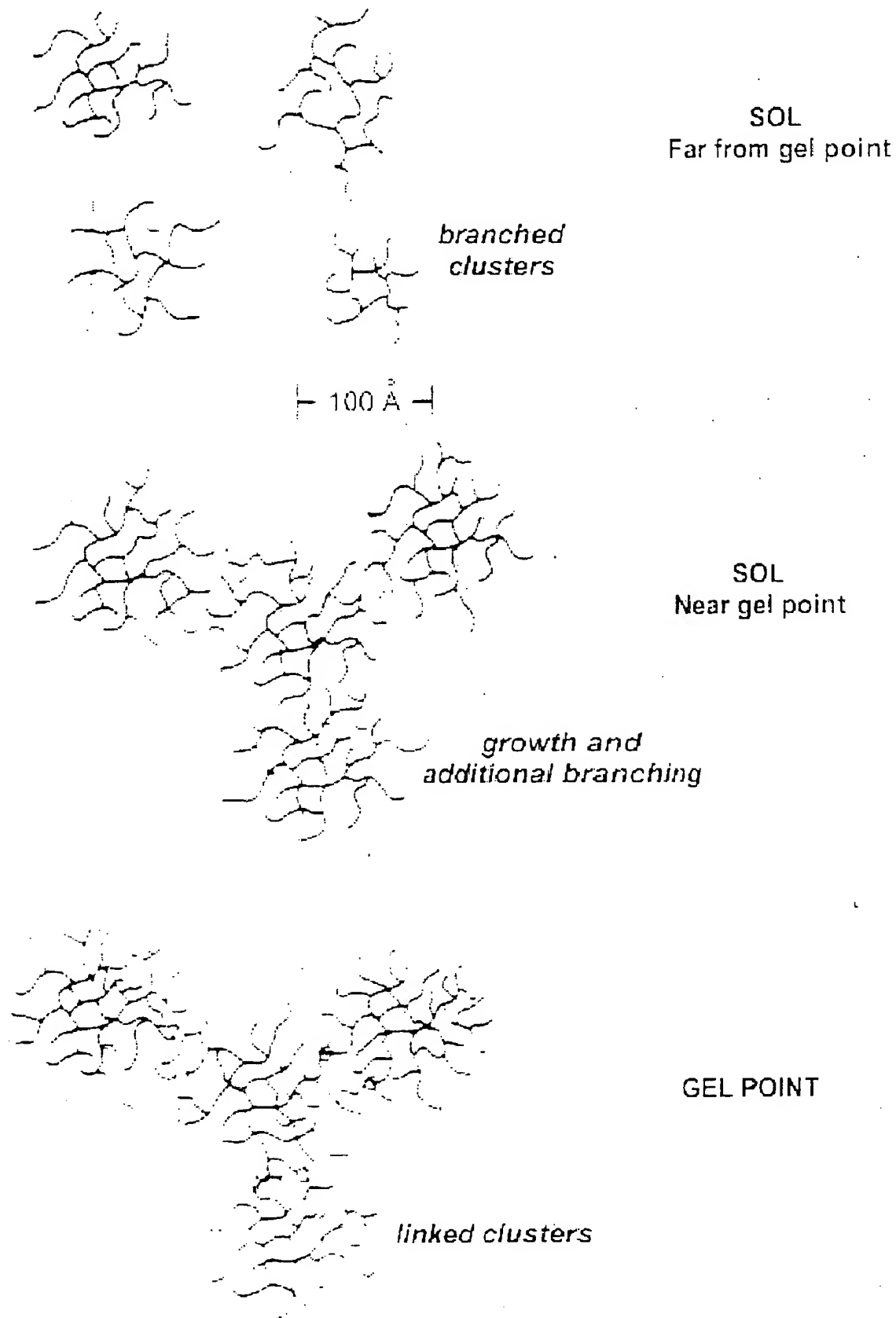- ◆ The kinetics and mechanism of intercalation
- ◆ Synthetic methods

6 ■ 2-D hybrid organic-inorganic materials based on organic polymers intercalated in layered inorganic solids

- ◆ Intercalation of a preformed polymer
- ◆ Monomer intercalation and *in situ* polymerization

7 ■ Core-shell hybrid organic-inorganic particles

- ◆ Filling up techniques of polymer shells
- ◆ Encapsulation processes of inorganic particles

But for higher alkoxysilane concentrations : « colloidal » gel

SOL
Far from gel point

branched
clusters

⊢ 100 Å ⊣

SOL
Near gel point

growth and
additional branching

GEL POINT

linked clusters

Figure 4 : Polymer growth and gel formation in base-catalyzed systems (colloidal gel)

Sol-gel chemistry and engineering background

Solid state reactions : precursors are thoroughly ground, mixed together and heated at high temperature. This procedure has to be repeated several times until an homogeneous product is obtained. Then, the materials have to be transformed into the desired shape : *single crystal, film, fiber, fine powder…*

Sol-gel synthesis : a new approach to the preparation of glasses and ceramics :

■ the metal-organic route with metal alkoxides in organic solvent

■ the inorganic route with metal salts in aqueous solution (chloride, oxychloride, nitrate..) : much cheaper and easier to handle than metal alkoxides, but their reactions are more difficult to control

1 – General mechanisms in the metal-organic route

Based on the growth of **metal oxo polymers** in a solvent

> ➤ inorganic step polymerization reactions through hydrolysis and condensation of metal alkoxides $M(OR)_z$, where M = Si, Ti, Zr, Al, Sn, Ce…, OR is an alkoxy group and Z is the valence or the oxidation state of the metal

> ➤ first step : hydroxylation upon the **hydrolysis** of alkoxy groups :

$$M\text{-}OR + H_2O \rightarrow M\text{-}OH + ROH$$
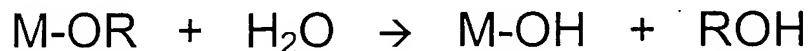
> ➤ second step : polycondensation process leading to the formation of branched oligomers and polymers with a metal oxo based skeleton and reactive residual hydroxo and alkoxy groups ; 2 competitive mechanisms :

■ **oxolation** : formation of oxygen bridges :

$$M\text{-}OH \;+\; XO\text{-}M \;\rightarrow\; M\text{-}O\text{-}M \;+\; XOH$$

where $X = H$, generally when **hydrolysis ratio h** = $H_2O/M \gg 2$
or $X = R$, when $h = H_2O/M < 2$

■ **olation** : formation of hydroxo bridges when the coordination of the metallic center is not fully satisfied $(N - Z > 0)$:

$$M\text{-}OH \;+\; HO\text{-}M \;\rightarrow\; M\text{-}(OH)_2\text{-}M \qquad \text{where } X = H \text{ or } R$$

The kinetics of olation are usually faster than those of oxolation

➢ formation of a metal oxo macromolecular network :

■ a **sol** where the polymerized structures do not reach macroscopic sizes

■ a **gel** when the recombination of the metal oxo polymers can produce bushy structures which invade the whole volume inside which the solvent, reaction by-products and free polymers are trapped

■ a **precipitate** when the reactions produce dense rather than bushy structures

Depending on the control of the structures of these oxo polymers through

■ the hydrolysis ratio h

■ the use of catalysts, complexing ligands or nucleophilic reagents

■ the steric hindrance of the alkoxy groups

■ the nature of solvents

■ the temperature

2 – Chemical reactivity of metal alkoxides

$$M(OR)_n + m\ XOH \rightarrow [M(OR)_{n-m}(OX)_m] + m\ ROH$$

where X stands for H (hydrolysis), M (condensation) or L (complexation by an organic ligand L)
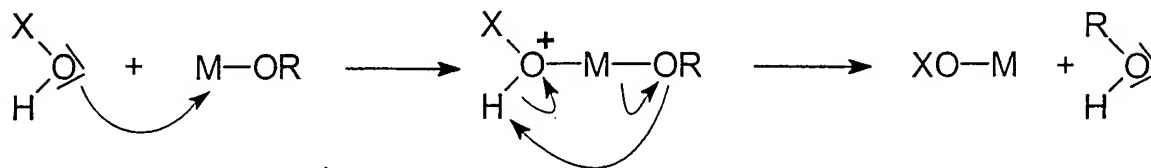
oxidation state :	Z	Z-1	Z
coordination number :	N	N+1	N

Consequently, the chemical reactivity of metal alkoxides toward nucleophilic reactions mainly depends on :

■ the strength of the nucleophile

■ the electrophilic character of the metal atom (an electronegativity-related property characterized by the positive charge on the metal atom)

■ its ability to increase its coordination number N : the degree of unsaturation of the metal coordination can be simply expressed by the difference N - Z, where N is the coordination number usually found in the oxide and Z is the oxidation state

alkoxides	χ	partial charge δ	ionic radius (Ǎ)	oxide	N	N - Z
$Si(OPr^i)_4$	1.74	+ 0.32	0.40	SiO_2	4	0
$Sn(OPr^i)_4$	1.89		0.60	SnO_2	6	2
$Ti(OPr^i)_4$	1.32	+ 0.60	0.64	TiO_2	6	2
$Zr(OPr^i)_4$	1.29	+ 0.64	0.87	ZrO_2	7	3
$Ce(OPr^i)_4$	1.17	+ 0.75	1.02	CeO_2	8	4

For similar alkoxy groups OR :

$$Si(OR)_4\ <<<\ Sn(OR)_4$$

$$\text{and}\quad Ti(OR)_4\ <\ Zr(OR)_4\ <\ Ce(OR)_4$$
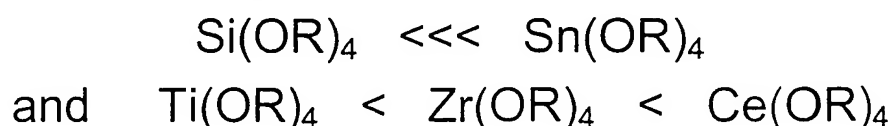
- **silicon** : relatively low electrophilicity and N - Z = 0 ; thus, silicon alkoxides are not very reactive : hydrolysis-condensation reaction rates must be increased by catalysts

- **tin** : higher electrophilic power and higher degree of unsaturation N – Z

- **titanium, zirconium and cerium** : lower electronegativity, but very high degree of unsaturation N – Z

Hydrolysis and condensation reactions of non-silicate metal alkoxides must be controlled by using chemical additives

a) reactivity of silicon alkoxides (N = Z = 4)

SN$_2$ mechanism : involving a hypervalent silicon transition state (penta- or hexacoordinated metallic center)

- the rates of hydrolysis and condensation increase under pressure without affecting the distribution of hydrolyzed or condensed species

- the reactivity of silicon alkoxides decreases when the size of the alkoxy group increases because of steric hindrance factors

Under acidic conditions (e.g. with mineral acids), the hydrolysis reaction is speeded up more efficiently than the condensation reaction :
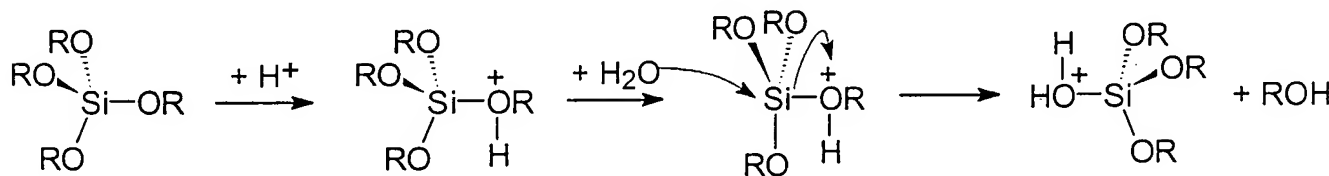

protonation of the alkoxo group, making alcohol a better leaving group

Condensation involves the attack of silicon atoms carrying protonated silanol species by neutral ≡Si-OH nucleophiles

- acidic conditions further the formation of protonated silanol species, but inhibit some nucleophiles

> the most basic silanol species (the most likely to be protonated) are those contained in monomers or weakly branched oligomers :
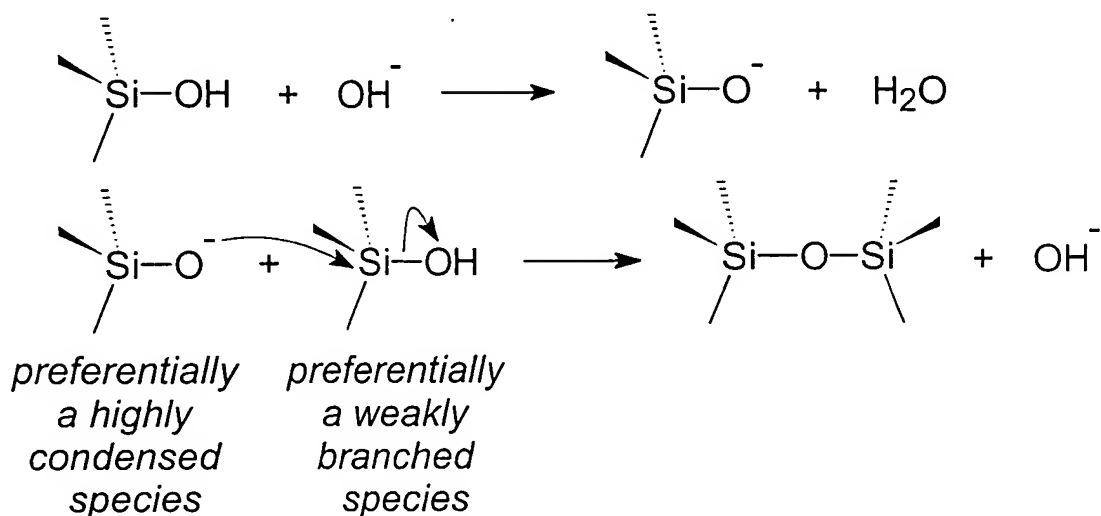

preferentially a monomer
or the end-group of a macromolecule
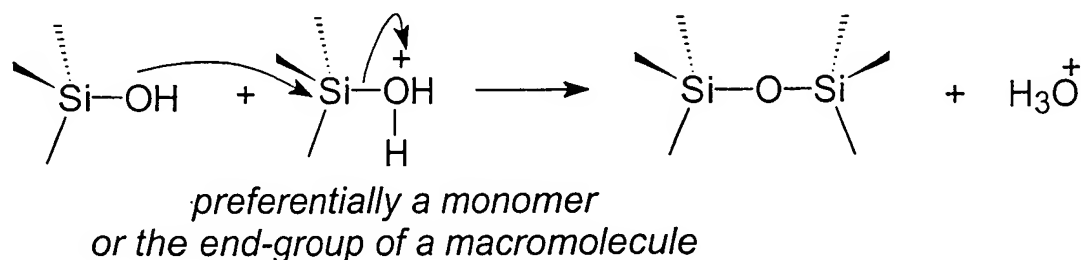
So a bushy network of weakly branched polymers is obtained

Under basic conditions (e.g. with ammonia), hydroxyl anions (OH^-) and deprotonated silanol ($\equiv Si\text{-}O^-$) are better nucleophiles than water and silanol species

> a fast attack at the silicon atom and both hydrolysis and condensation reactions occur simultaneously

The condensation involves the attack of a deprotonated silanol ($\equiv Si\text{-}O^-$) on a neutral siloxane species

> the acidity of silanol increases when -OH or -OR groups are replaced with $-O\text{-}Si\equiv$ groups because of the reduced electron density on Si atom

preferentially	*preferentially*
a highly	*a weakly*
condensed	*branched*
species	*species*

The result of basic catalysis is an **aggregation** (monomer-cluster) that leads to more compact highly branched silica networks, that are not interpenetrable before drying and thus behave as discrete species

· The nucleophilic activation by Lewis bases (dimethylamino-pyridine, n-Bu$_4$NF, NaF…) is also efficient for both hydrolysis and condensation reactions, which occur simultaneously as for basic catalysis

> ➤ reversible formation of a pentavalent intermediate with F⁻ that stretches and weakens the surrounding ≡Si-OR bonds

> ➤ the positive charge of the silicon atom increases, rendering the silicon atom more prone to nucleophilic attack

Highly branched silica networks are obtained.

b) reactivity of non-silicate tetravalent alkoxides (Z = 4)

Very sensitive to moisture, they must handled with care under a dry atmosphere otherwise precipitation occurs

Coordination expansion : self regulation of their reactivity by increasing the number of coordinating molecules using their vacant orbitals to accept electrons from nucleophilic ligands
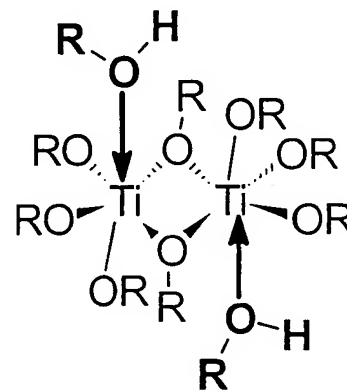
> ➤ occurs by alkoxy bridging or solvation :
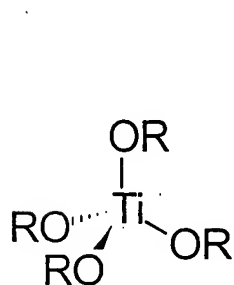

monomer
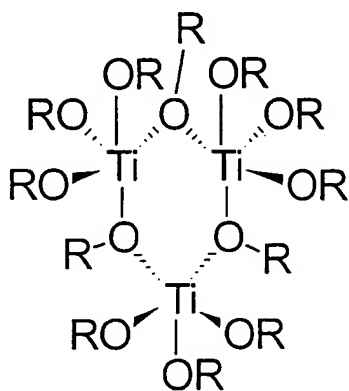
trimer
in pure benzene

dimer
in alcohol

> ➤ the molecular complexity depends on concentration, temperature, solvent, oxidation state of the metal, steric hindrance of the alkoxy groups

> it increases with the atomic size of the metal atom and decreases with increasing bulkiness of the OR groups

> in non-polar solvents, the molecular complexity of alkoxides is higher than in their parent alcohol, and therefore their hydrolysis reaction is slower and leads to the formation of clear gels

Control of the reactivity with inhibitors : **inorganic acids**, β-**diketones, carboxylic acids** or other complexing ligands which inhibit condensation reactions and therefore prevent precipitation, force the growth to a gel state or stop growth

ex : **acetylacetone (AcacH)** leads to less hydrolyzable M-Acac bonds : molecular clusters, chain polymers or colloidal particles depending on

- the hydrolysis ratio $h = H_2O/M$
- the complexation ratio $x = Acac/M$
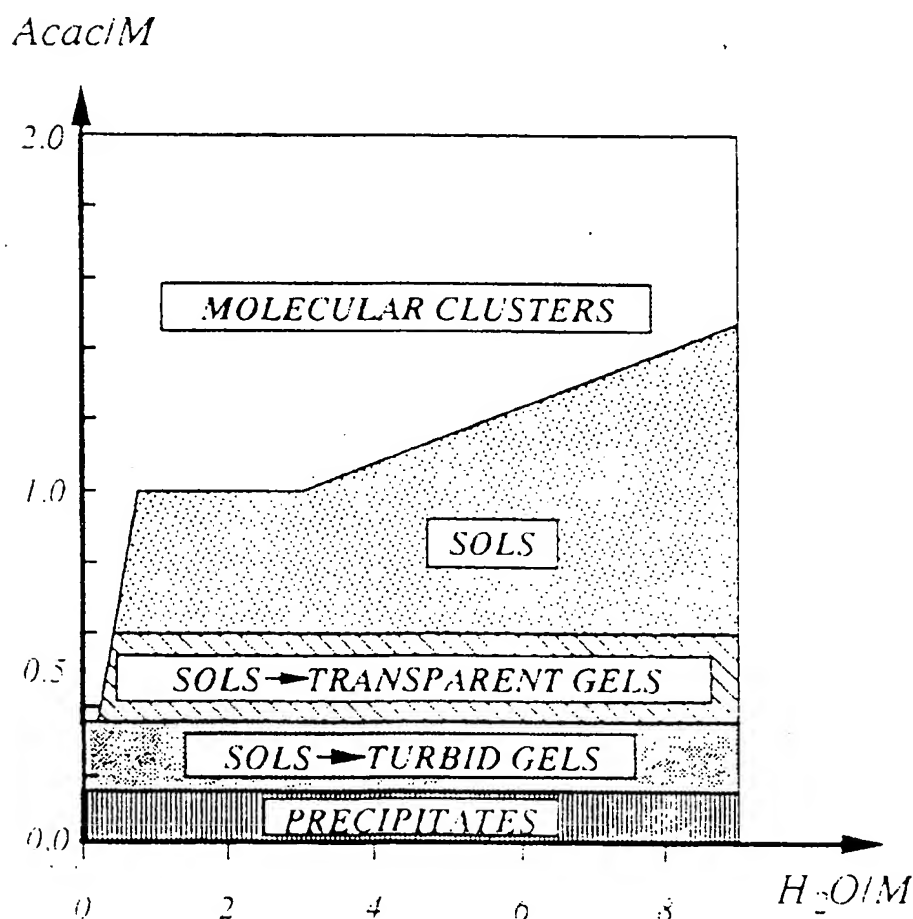
Figure 1 : State diagram describing the hydrolysis-condensation behavior of complexed tetravalent metal alkoxides

c) reactivity of different metal alkoxide combinations

Phase separation : ex : $Ti(OBu)_4$ generally reacts rapidly with water and precipitates out of the reaction mixture before it can react with $Si(OEt)_4$ network
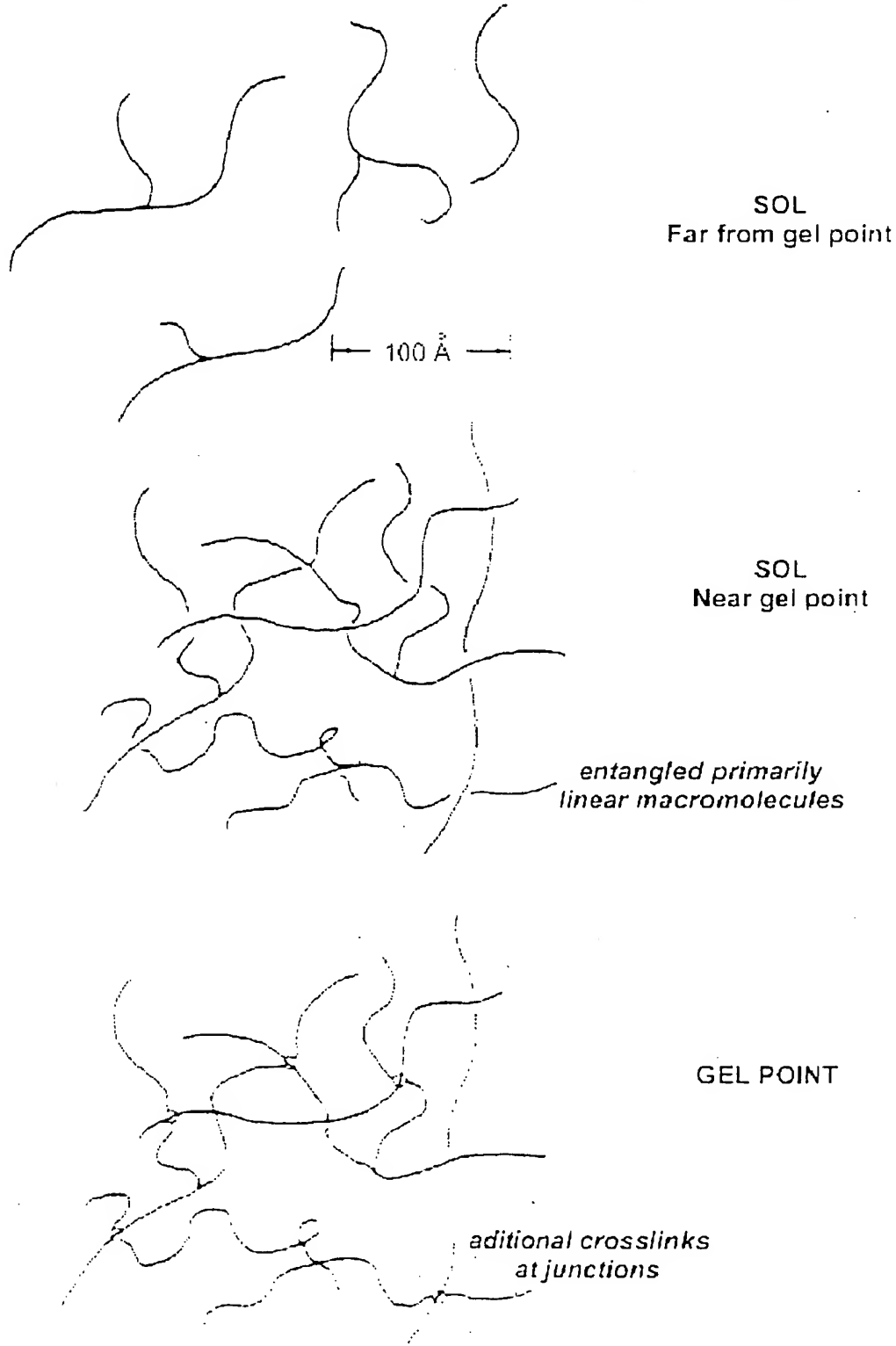
> ➢ allowing $Si(OEt)_4$ species to prehydrolyse in the presence of water and an acid catalyst. Then, fast-reacting $Ti(OBu)_4$ is added ; it quickly hydrolyzes and at least partially condenses into the preexisting immature $Si(OEt)_4$-based network

3 – <u>Gelation, aging, drying and firing</u>

We focus on the mechanisms in silicate systems

a) gelation

Under acid catalyzed conditions : « polymeric » gel

SOL
Far from gel point

├─ 100 Å ─┤

SOL
Near gel point

*entangled primarily
linear macromolecules*

GEL POINT

*aditional crosslinks
at junctions*

Figure 2 : Polymer growth and gel formation in acid-catalyzed systems (polymeric gel)

Under basic conditions and/or with higher additions of water (e.g. $h \geq 7$) : more highly branched clusters which do not interpenetrate prior to gelation and thus behave as discrete species.

If the total concentration of alkoxysilane is low (< ~0.3 M) gelation leads to the formation of colloidal silica (Stöber process).
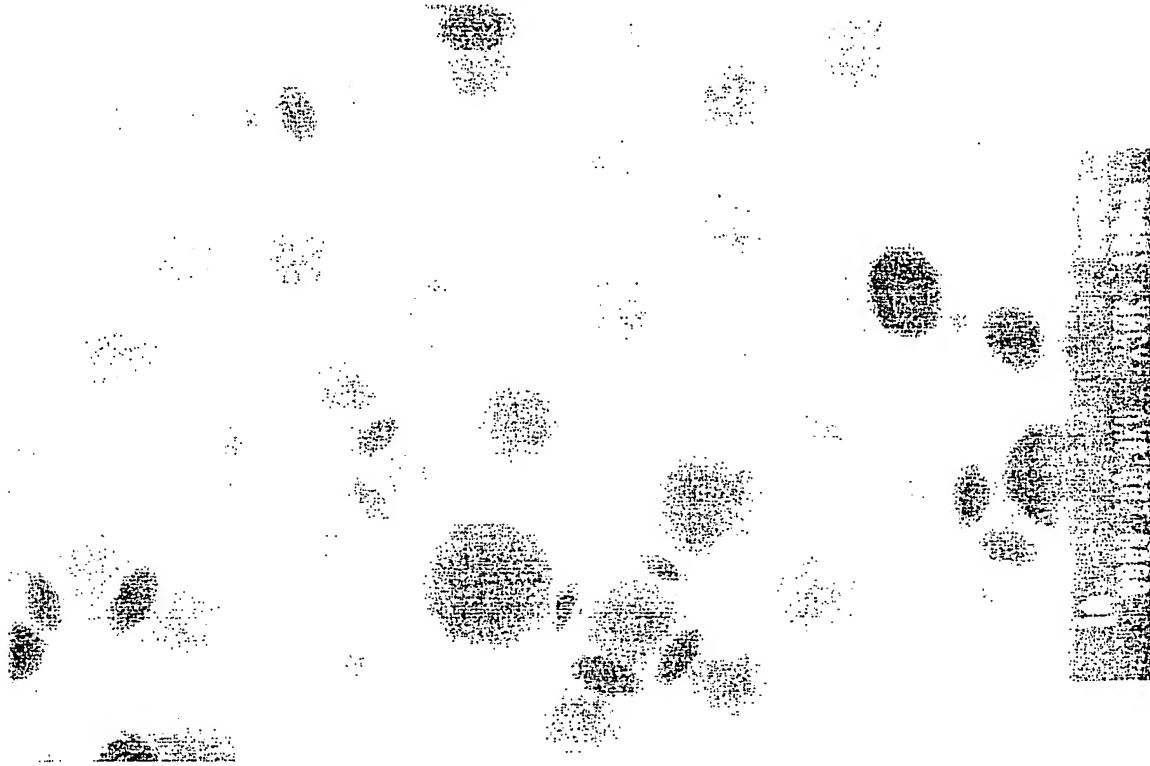
Figure 3 : TEM imaging of colloidal silica obtained through Stöber process

b) aging

Gelation : freezing in a particular structure (i.e. may be considered as a rapid solidification process)

Aging : structure modifications with time depending on temperature, solvent and pH conditions

- ➢ gel separation into regions of high and low polymer density because it is expected that as the critical point is approached (e.g. during a change in concentration), fluctuations in polymer density grow larger in amplitude (than those resulting merely from thermal motions)

- ➢ promotion of additional crosslinking as unreacted terminal groups (OH and OR) come in contact in regions of higher polymer density

- ➢ acceleration of the phase separation process and creation of liquid-solid interfaces

- ➢ further structural changes attributed primarily to surface energy effects : it is well known that surfaces exhibiting positive radii of curvature dissolve more readily than surfaces exhibiting negative radii of curvature. Therefore as the dissolution rate is increased (e.g. by increased temperature or pH) dissolution-redeposition results in neck formation causing the gel structure to become fibrillar and the pore formation. Of course, when dissolution is extensive, the gel network would break down and ripen to form a colloidal sol.

c) drying (or desiccation)

Drying : removing of the solvent phase

Method influenced by the intended use of the dried material :

- ☐ if powdered ceramics are desired, no special care need be exercised to prevent fragmentation

- if **monoliths from colloidal gels** are desired, the drying procedures are largely determined by the need to minimize internal stresses associated with the volume changes on drying and the capillary forces in the gel pores :

  - ➤ during the initial stages of drying, the volume change of the gel is equal to the volume of evaporated liquid. The gel network is still flexible and can rearrange to accommodate the decreasing volume. All pores are filled with solvent and liquid-air interfaces are not present

  - ➤ as drying proceeds, the gel network becomes more restricted and the removal of liquid leads to the formation of such interfaces and the development of capillary stresses : the capillary pressure ΔP developed in a cylindrical capillary of radius r partially filled with a liquid of wetting angle θ, can be expressed by :

$$\Delta P = 2\gamma\cos\theta/r$$

  where γ is the surface tension. The development of cracks in a drying gel is shown on figure 5 :

(a)   (b)

$\Delta P_1 < \Delta P_2$

crack

crack
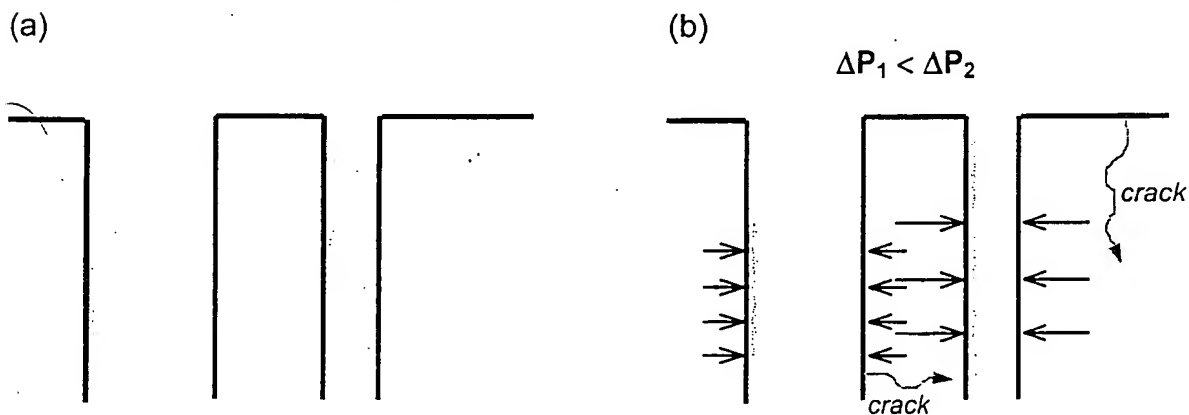
Figure 5 : Formation of differential strains at the pores during drying : (a) before and (b) after the onset of capillary forces.

When evaporation leads to the formation of menisci, the different radii of the pores cause unequal capillary pressures to generate differential stresses $\sigma_1 < \sigma_2$. If the stress difference $\sigma_2 - \sigma_1$ locally exceeds the strength of the gel network, a crack will result. The tendency toward fragmentation is thus determined by both the average pore size and the pore size distribution.

➤ generally, fractures associated with excessive capillary forces can be reduced or eliminated by :

■ strengthening the gel by reinforcement

■ enlarging the pores

■ reducing the surface tension of the liquid with the use of surfactants

■ making the interior surfaces hydrophobic

■ evacuating the solvent by freeze-drying

■ operating under hypercritical conditions : effected by heating the gel with methanol in an autoclave to temperatures and pressures exceeding the critical point of methanol (240°C/8.1MPa). A slow evacuation (3-4 hr) was followed by flushings with dry argon to eliminate the last traces of alcohol. This method produces dried gels with much larger pore volumes (aerogels : porosity of ~85 %, specific surface area of 250-600 $m^2.g^{-1}$ and pore size of 250-1250 Å) than conventional evaporative drying (xerogels : pore size ≤ 20 Å). Because of the absence of the liquid-vapor interfaces, no capillary forces arise to cause network collapse and shrinkage during drying

■ if **monoliths from polymeric gels** (such as those obtained by the acid catalysis of silicon alkoxide at low water contents) are desired : the polymeric species are weakly crosslinked and as solvent is removed, they can deform readily and form a dense gel structure while polymer itself shrinks and forms more crosslinks

➤ dense dried gel with no large voids

d) firing

Firing : heating to convert the dried gel to a dense ceramic. For silica gels, the following reactions occur :

- ➤ desorption of physically adsorbed solvent and water from the walls of micropores (100-200°C)
- ➤ decomposition of residual organic groups into CO_2 (300-500°C)
- ➤ collapse of small pores (400-500°C)
- ➤ collapse of larger pores (700-900°C)
- ➤ continued polycondensation (100-700°C)

☐ if **powdered ceramics** are desired, no special care need be exercised to prevent fragmentation. Attention must, however, be directed to the removal of organics to avoid undesirable bloating, foaming or blackening

☐ if **monolithic ceramics** are desired, special care must be taken to ensure complete removal of water, organic groups or decomposition products, prior to micropore collapse to avoid the development of stresses leading to fragmentation

- ➤ for the production of large monoliths of SiO_2, poly-condensation has to be completed prior to pore collapse
- ➤ with non-optimized firing schedules, residual organic groups and H_2O can lead to blackening and fragmenta-tion, as well as to the formation of bloated and foamed samples (in cases where foams are desired, specific agents such as urea can be used in forming the gel)

Sintering and densification phenomena also take place, via typical sintering mechanisms such as evaporation condensation, surface diffusion, grain boundary and bulk diffusion. The small particle size of the powders lead to high reactivities and enhanced sintering and/or coarsening rates (the principal process involved in densification is often viscous sintering)

4 – <u>Applications and limitations of sol-gel techniques</u>

a) advantages

Sol-gel processes allow the synthesis of ceramics of

■ **high purity**, because organometallic alkoxy precursors can be purified by distillation or recrystallisation

■ **high degree of homogeneity**, because reagents are mixed at the molecular level

■ **low or high porosity**, by using appropriate heat treatment and firing times

The veritable explosion of interest in this area seems to result in large measure from the perceived technological opportunities :

■ the ability to prepare glasses of materials which cannot be obtained as amorphous solids by cooling from the liquid state

■ the capability of obtaining fully-dense amorphous solids at temperatures lower by hundreds of centigrade degrees than those required for conventional compaction/densification or for melting

■ the possibility of obtaining fully-dense crystalline ceramics which cannot be prepared by conventional powder processing

■ the ability to obtain materials with novel distributions of phases contained therein...

b) drawbacks

■ high cost for the majority of alkoxide precursors
■ long processing times
■ volatiles production
■ shrinkage
■ development of stresses leading to fragmentation

c) applications

☐ **novel glasses** produced from gel precursors in three ways :

    ○ melting gel-derived powders : gel-derived powders are used as batch ingredients for glass melting primarily because of the high degree of chemical homogeneity which they offer. This leads to shorter melting times and lower melting temperature as well as compositional uniformity

    ○ sintering or hot pressing gel derived powders : the key to glass formation is the development of an appropriate heat treatment schedule to remove the residual organic groups and achieve pore collapse without inducing crystallization in the sample

    ○ heat treating gels to produce monoliths (already described)

The physical properties of gel-derived glasses are usually closely similar to those of glasses obtained from the melt. The most attractive feature is the development of novel glass compositions : $CaO\text{-}SiO_2$ or $Na_2O\text{-}ZrO_2\text{-}SiO_2$ with high ZrO_2 content, which simply cannot be obtained from the melt because the cooling rate must be very high to avoid detectable crystallization.

☐ **fibers** : using appropriate hydrolysis conditions, continuous fibers may be drawn from solutions of metal alkoxides and converted to glass fibers by heating (ex : $ZrO_2\text{-}SiO_2$ or $Na_2O\text{-}ZrO_2\text{-}SiO_2$). Fibers can also be prepared by extruding gelled solutions (colloidal as well as polymeric gels) through dies of appropriate diameter (ex : polycrystalline alumina, microcrystalline $Al_2O_3\text{-}Cr_2O_3\text{-}SiO_2$, mullite $3Al_2O_3 \circ 2SiO_2$, aluminum borosilicate $3Al_2O_3 \circ B_2O_3 \circ 3SiO_2$)

☐ **abrasives** : after gelation and drying, the material is crushed (a simple process with frangible dried gel) and sized. The sized powders are then fired. In this way, Al_2O_3 abrasive

• particles with uniformly dispersed ZrO_2 particles and a very fine grain size (< 300 nm) can be obtained. Such abrasive particles have superior grinding performance compared with fused or sintered Al_2O_3-based abrasives in a number of applications

■ **thin films and coating** : the permissible drying rates, consistent with the avoidance of fracture, were evaluated and found to vary inversely with the thickness of the body being dried. This limitation leads naturally to the main use of gels in **coating applications**, where the thickness are small and the drying rates can be correspondingly high. Four techniques are mainly used for film deposition onto substrates :
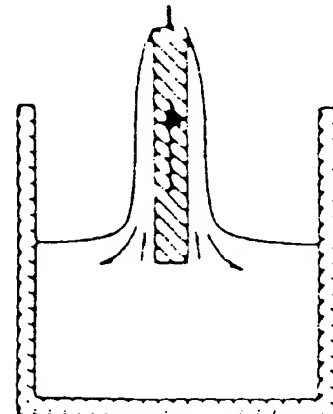
● **dipping** (the most widely used), where the part to be coated is withdrawn from a solution. The faster the substrate is withdrawn, the thicker the deposited film
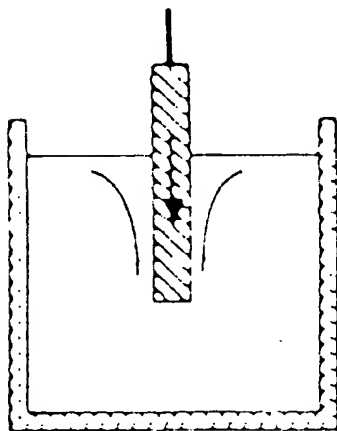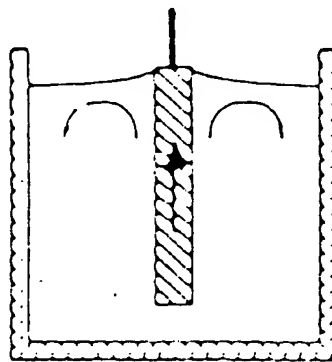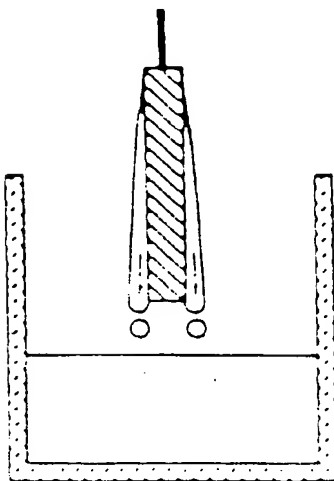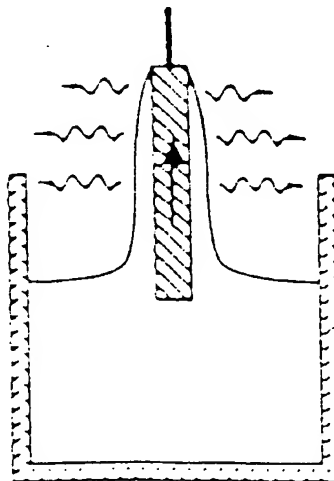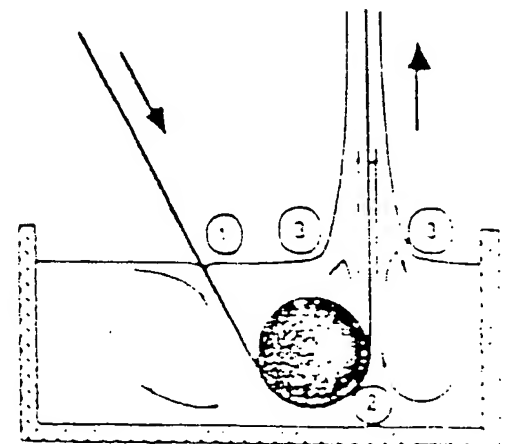

IMMERSION   START-UP   DEPOSITION & DRAINAGE

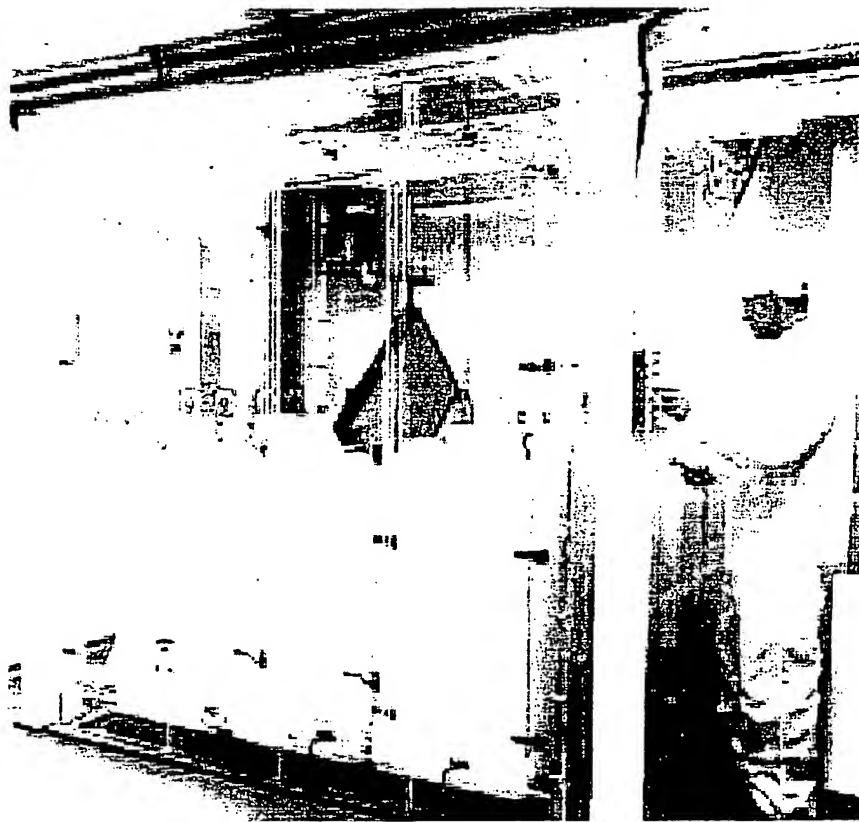DRAINAGE   EVAPORATION   CONTINUOUS
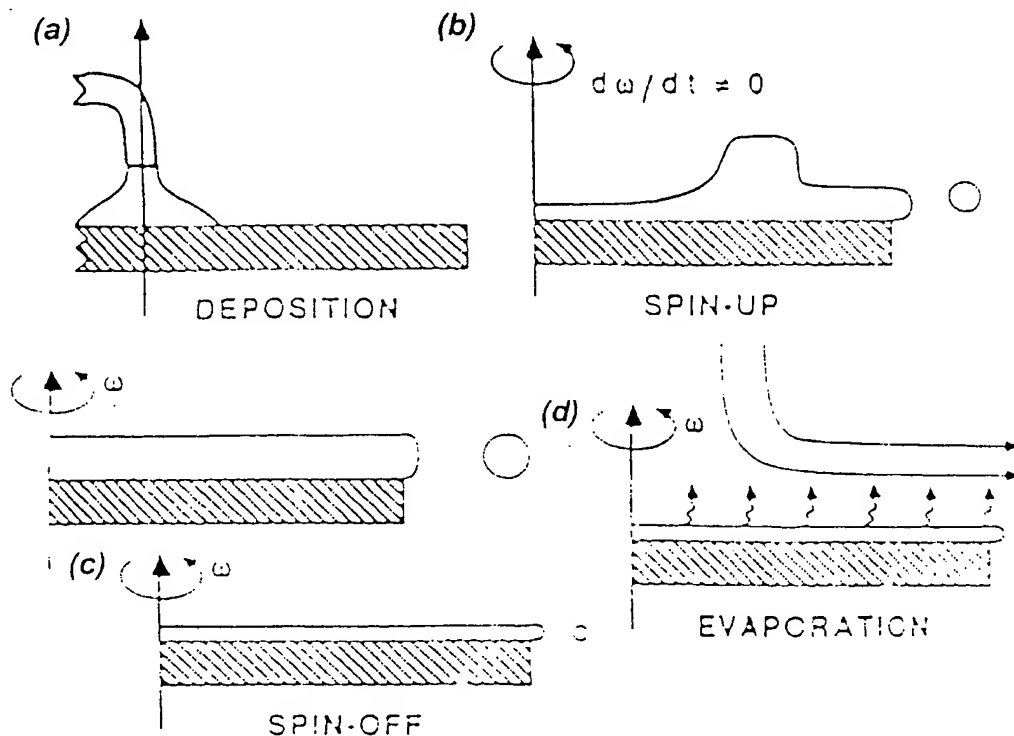
Figure 6 : Industrial dip-coating system

● **lowering**, where the object remains at rest and the liquid level is lowered

● **spinning**, where the liquid film is spread out by spinning the wetted surface. Advantages : the uniform thickness of the film due to the spin-off stage and the deposition onto small substrate from a small quantity of sol

● spraying, where the surfaces are sprayed with fine disperse solutions. This process has difficulty in maintaining strict tolerances and is thus used mostly for protective coatings.

Some of the coating-type applications which seem well-suited for sol-gel techniques include :
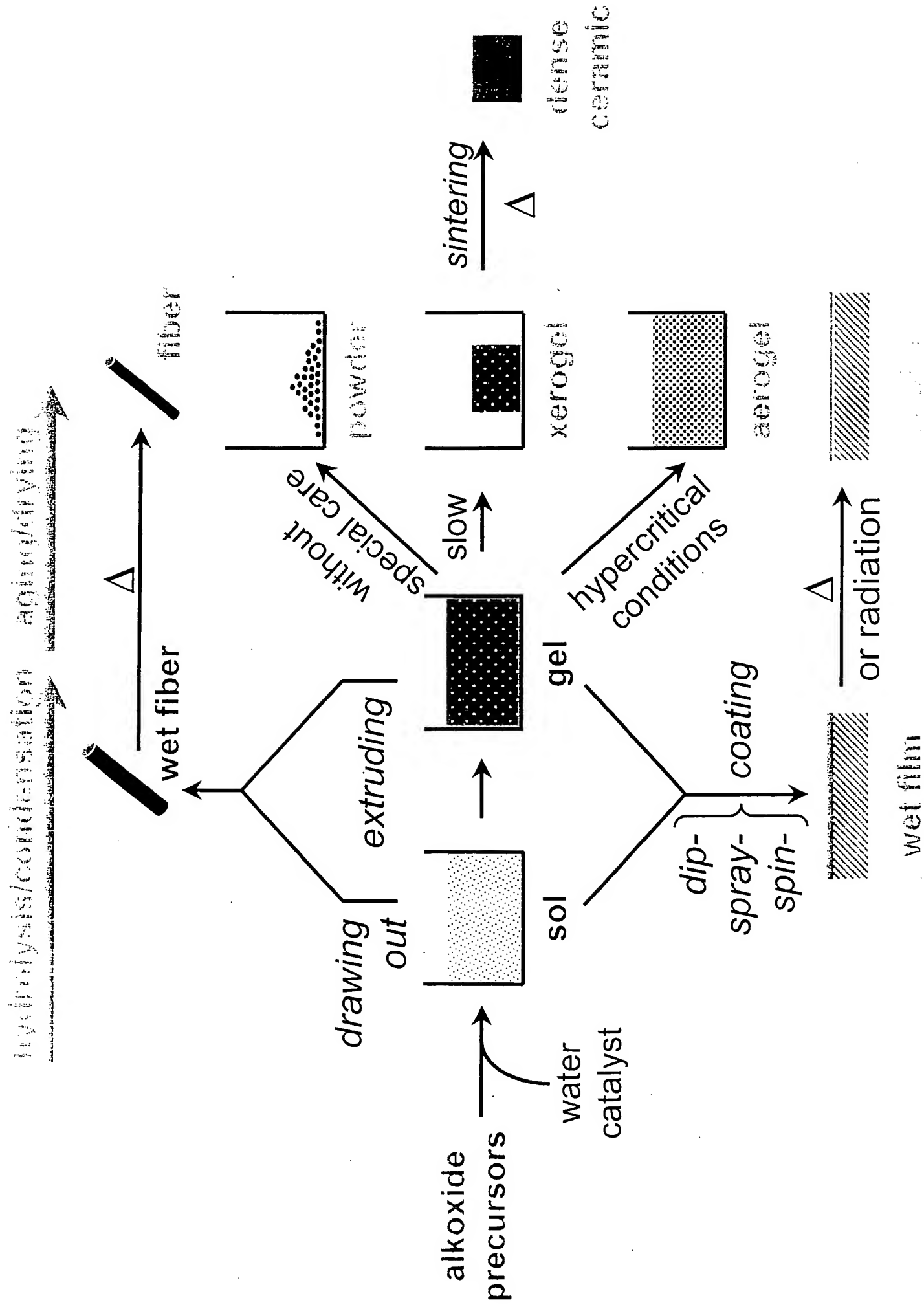
■ antireflection coatings (single layer or multilayer films)

■ absorbing coatings

■ filters for lighting and optical purposes

■ semiconducting coatings

■ protective layers (both chemical and thermal)

■ independent films, prepared by

> pouring alkoxide solutions onto liquids which do not mix with the solution and allowing the film to hydrolyze

> pouring the solution onto non-wetting surfaces such as Teflon

> forming films using wire rings with solutions of appropriate viscosity

d) conclusion

Sol-gel chemistry is still in its infancy and a better understanding of the basic inorganic polymerization chemistry has still to be reached before a real mastery of the process can be obtained.

Nevertheless this low temperature processing may be exploited. As a result, the incorporation of organic materials into sol-gel-derived oxides becomes possible

summary of sol-gel process, techniques and products

alkoxide precursors

water catalyst

drawing out

sol

extruding

dip- spray- spin- coating

wet fiber

wet film

Δ

gel

hydrolysis/condensation

aging/drying

fiber

Δ

slow

without special care

hypercritical conditions

or radiation

Δ

sintering

powder

xerogel

aerogel

dense ceramic

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Colloids

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Introduction

There should be a more exciting name for the phenomena to be discussed here. The dull term *colloid* that reminds us of glue is, nevertheless, the accepted word. It was coined in the early 19th century by the Father of Physical Chemistry, Thomas Graham (1805-1869), to distinguish those materials in aqueous solution that would not pass through a parchment membrane from those that would. Glue was indeed a material that would not, and the Greek for glue is *kolla*, from which we also get "protocol" and "collagen." Those that would pass through were things like salt, and other soluble crystalline substances, which Graham called *crystalloids*. As we shall see, the field is much, much richer than this.

Colloids received little attention until the end of the century, when van't Hoff, Oswald and Nernst founded modern physical chemistry and they, and others, became fascinated by colloid phenomena. There had been famous observations by Tyndall and others in the meantime, but chemists could not get excited over glue. Then, in the 1920's and 1930's, the importance of colloids to industrial processes and biochemistry changed everything. Colloids became a hot field, and soon every elementary textbook said something about them. In writing some of the other articles on the site recently, I became gradually aware of the fascinatic   it my knowledge of them was very deficient. This article is the result, and I hope what colloids are all about, and demonstrate how interesting and useful they are

An interesting philosophical point was suggested by this study. Colloids are oft $Calvert$ r," and I wondered just how meaningful this concept is. We shall find that it is ver concept concerning colloids in a word, though heaven knows chemists have tri coined. It is necessary to name things to think about them efficiently, and one t assiduously is to assign names. Biology comes to mind, with endless terms and appearances, at least until recently. Naming gives the appearance of knowledge, where there is no real knowledge at all. The antithesis to mere naming is mathematical analysis, which gives real conclusions and effective knowledge. The danger of names comes when they are regarded as real things and are used to delimit instead of simply to denote and describe.

It is easy to recognize the three conventional states of matter in ice, water and steam. The names solid, liquid and gas can be attached to certain suites of properties, and makes a useful distinction. In a gas, particles of the substance move freely and have to be stopped by walls. In a liquid, the particles are sometimes associated, sometimes not, but always occupy a certain volume. In a solid, the particles cannot move far relatively, and can only vibrate. Many substances can be classified by these properties, but the terms do not separate matter into three mutually exclusive boxes, and may not be descriptive enough. Where is tar, for example, or jelly, or a substance above its critical point? Colloids will give many examples of substances for which the simple classification into three states is wholly inadequate.
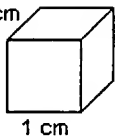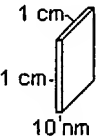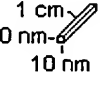
The properties of matter depend almost completely on its structure. All metals are alike, to a good approximation. They are shiny, soft, tough substances that conduct electricity. All ionic crystals are alike (granted differences in crystal symmetry). They are hard, transparent and do not conduct electricity in the solid state. They can usually be crushed into white powders. The variations between metals, or between ionic crystals, are very much less important than their similarities. Saying that a substance is a metal, or an ionic crystal, says much more than simply that it is a solid. Solidity is only a macroscopic appearance, of no fundamental significance, like being green.

I have seen the definition of matter as "that which occupies space." But what about gases? They occupy space, of course, but two or more gases can occupy the *same* space, as far as appearances go. The important thing is to use terms like solid, liquid, gas only as far as they are useful descriptions, and not consider them as exclusive classifications into which everything must fit. To see that this is not trivial, consider the many sciences (not generally chemistry or physics) in which there are bitter controversies about which named category to assign to some object or process. We should not be limited by the arbitrary names we give our concepts.

Properties of Colloids

I recalled that colloids were particles larger than molecules, but smaller than grains of sand. This is true, and colloidal dimensions can be considered to be from about 10 nm up to 1000 nm, or 1 µm, but mere size is not the important thing about colloids. The overwhelmingly important property of colloids is that they have very large surface area. To some degree, they are *all surface* and their properties are those of their surfaces. I do not remember appreciating this properly before, but I can assure you of its significance. Incidentally, 1 µm is about the size of a bacterium. I shall use the word "colloid" to refer to a substance of colloidal dimensions, or to a colloidal system, indifferently.

To see the significance of this observation, consider the cubic centimeter in the diagram at the right. In this form, it has an area of 0.0006 m^2. We could say that it is almost all volume. Most of its molecules are safely resident behind its surface, secure from disturbance or attack. Let us now divide it into thin laminae, 10 nm thick, a colloidal distance. The cube becomes a million laminae, with a total surface area of 200 m^2. Every molecule is now only a short distance from the cold outdoors, and the material is all surface. We have turned the mass cube into a *laminated colloid* by this delicate slicing alone.

	State of Subdivision			
	mass	laminated	fibrillar	corpuscular
N	1	10^6	10^{12}	10^{18}
A_1, m^2	6×10^{-4}	2×10^{-4}	4×10^{-10}	6×10^{-16}
A, m^2	6×10^{-4}	200	400	600

State of Subdivision and Total Area

Continuing, we now slice each of the million laminae into a million fibers, and the surface area doubles. We still have a colloid, of course, with two dimensions colloidal, but have not increased the area greatly, not as we did in the first slicing. We can expect *fibrillar* colloids as well as laminar ones. Finally, each fiber is chopped into a million bits, giving a *corpuscular* colloid. This increases the surface area only by 50%, to 600 m^2. From the mass to the corpuscle, the surface area has been increased by a factor of a million, which is typical of a colloid. Note that most of this increase came with the first dimension to "go colloidal," so we can call anything with any least dimension of colloidal size to be a colloid. This was another thing that I did not appreciate in my ignorance.

The large area emphasizes surface effects relative to volume effects, giving colloids different properties than those of bulk matter. The surface tension of a liquid is the free energy required per unit area to create new surface. For water against air, its value at 20°C is 72.75 dyne/cm. For mercury against air, it is 450 dyne/cm. For mercury against water, it is 375 dyne/cm, not surprisingly close to the difference of the other two values. The ratio of surface to volume for a sphere of diameter d, or a cube of side d, is 6/d. The surface energy of small drops will strongly affect their properties. If a cubic centimeter of water were divided into 10 nm cubes as above, the coalescence of the cubes would release enough surface energy to heat the water by about 10°C. A cubic centimeter of mercury would be warmed by 143°C by the same procedure.

It is better to define a colloid as a system in which the surface area is large and in which surface effects are predominant, rather than simply in terms of particle size. Indeed, in foams there are no colloidal particles at all--it is the thinness of the films that creates the colloidal behavior. Similarly, in a gel the fibrous structure is what is colloidal. In any colloidal system, there must be at least one structural dimension of colloidal size in order for the large surface area to exist in a limited volume, however. This broadened definition of colloid is not only reasonable, it is useful. A colloid is a material system that is mainly surface.

The next important characteristic is that a colloid is a *two-phase* (at least) system. A *phase* is a homogeneous component of a system, in the sense of the Phase Rule. The Gibbs Phase Rule applies to systems in which the phases have negligible surface energy, which is perfectly applicable to phases that are "all volume" as our centimeter cube was, or even to phases of microscopic dimensions (larger than 1μm). It does not apply to the system of colloid phases, in which surface energy predominates. Therefore, be careful when applying the Phase Rule to colloidal systems.

A colloidal system consists of an *internal phase*, which is the material of colloidal dimensions, and an *external phase*, which is the material in which the colloid is dispersed. These designations are analogous to the terms *solute* and *solvent* used for simple solutions (which form a single Gibbs phase). As the particles of a corpuscular colloid become smaller and smaller, we go over imperceptibly from a two-phase colloid to a single-phase solution, and there is no definite boundary. This gives a hint as to why I discussed names and their significance in the introductory paragraph.

The colloidal system that is most similar to a simple solution is a dispersion of corpuscles, or particles, in a liquid. This is called a *sol*, and the liquid is the external phase. This is the classical colloid as described by Graham. If the external phase is a solid instead of a liquid, the system is called a *solid sol*. The only difference is the mobility of the molecules. In a solid sol, they can move only by diffusion. If the external phase is a gas, usually air, instead of a liquid, we have an *aerosol*. There is no definite boundary between a sol and a solution, but still they are significantly different. There is also no definite boundary between a sol and a coarse suspension. A coarse suspension will settle out rapidly, while a sol may be permanent.

The particles that appear in a sol may be wetted by the liquid, or may not. Wetting is a typical surface effect, and so is of paramount importance in a colloid system. In the first case, the liquid is *adsorbed* on the surface of the particle. The terms *adsorb* and *absorb* sound alike, but are quite different. A substance that is absorbed is taken into the volume of the absorbing substance, like water into sand. If is is adsorbed, it attaches itself only to the surface. Since colloids are all surface, as we have pointed out, adsorption is what is important with them. If the particle adsorbs the external phase, it is called *lyophilic*, or *hydrophilic*, if the external phase is water. The Greek verb "luo" means to dissolve or destroy, and philic is from "philos," love. A lyophilic colloid "loves the external phase." On the other hand, if the particle does not adsorb the external phase, is is said to be *lyophobic*, or "fears the external phase."

Sols that contain inorganic particles, such as metals, are mostly lyophobic, as are most aerosols and solid sols. Lyophobic hydrosols are a very common kind of colloid, and deserve detailed description. For example, consider the hydrosol of gold with particles about 4 nm in size. This was one of the first sols studied extensively, and has interesting properties. With about 0.1% gold, the sol is a rich ruby red. The similar solid sol in glass makes ruby glass. The gold particles absorb strongly in the green and blue, so the transmitted light is red. There is a little yellow-green scattered light, but mostly it is a case of absorption by the gold metal. If the gold particles clump together, which they may do as time passes, the color of the solution changes. When the particles are about 40 nm in diameter, the solution is blue, with considerable scattered light. If the particles agglomerate further, the color disappears and gold flakes settle out.

Bacteria, which are about 1 μm in diameter, can be suspended in water to form a sol, which has all the classic properties. The Brownian motion, the Tyndall effect (turbidity), and even electrophoresis are seen. The bacteria act as a hydrophobic sol, peptized by their electrostatic charge. The properties of a sol are largely independent of the nature of the internal phase.

There are two interesting questions here about the stability of the sol. First, what keeps the gold suspended in the red solution so that the tiny particles do not settle out? Second, how are the particles kept from agglomerating? Let's take the first question first. The gold particles fall under gravity through the water. The terminal velocity v of their fall is given by Stokes's equation, $(mg - m'g) = 6\pi\eta av$, where m is the mass of the particle, a its radius, m' the mass of the water displaced, and η is the viscosity of water (1.002 centipoise at 20°C). A correction factor $(1 + K\lambda/a)$ must be applied for the small particles, where K is a constant, λ is the mean free path of the liquid molecules (this factor really applies better to aerosols), and a is the radius of the particle. On the other hand, the particles are subject to the bombardment of the molecules of the liquid, which produces the Brownian movement. For a sufficiently small particle, the upward diffusion produced by the Brownian movement overcomes the gravitational fall, and an equilibrium is reached, much like the equilibrium of gases in the atmosphere. Perrin first verified this effect, although it is quite complicated in this case, the gas-like effect only occurring close to the upper surface of the sol. There is a *critical size* for a particle, below which it will not settle out. At any rate, this is why colloidal-size particles do not settle out of a sol.

Now for the second question. Generally, if two colloidal particles collide, they will stick together and make a bigger particle, because it is usually favored by energy. Eventually, the particles get larger than the critical size to be suspended by the Brownian movement, and they settle out. There must be some good reason if this is not to happen. In most lyophobic colloids, the particles are electrically charged with the same sign, and this keeps them apart, since they repel one another. The particles are charged mainly because they adsorb certain ions in the environment. In water, they may be OH^- ions, which are generally present, and give the particles a negative charge. The H^+ ions are hydrated, so are not as easy to adsorb, but apparently some particles like them, and become positively charged. If you try to make a hydrosol with particles of opposite charges, they neutralize each other and the sol collapses. Since lyophobic sols are stabilized by electric charge, adding electrolytes generally destroys the sol. When rivers reach the sea with their loads of colloidal sediment, the ions in sea water coagulate the sol, and the load is deposited in the delta. There are other ways for a particle to become charged. A zinc particle, for example, may become negative when some zinc dissolves according to $Zn \rightarrow Zn^{++} = 2e^-$, and the electrons remain on the particle.

How the charges are distributed is an interesting question. The sol appears electrically neutral on the large scale. The particle with its adsorbed charges is called a *granule*. The charges are in a thin layer on the surface. They attract an atmosphere of opposite charges from the external phase, just as an electron in a plasma surrounds itself with a shielding positive charge by attracting positive ions and repelling electrons. The whole neutral structure, granule plus mobile external charge, is called a *micelle*. This, then, is what moves around, the charged particle and its cloud of opposite charge. When we apply an electric field to the sol, the cloud of charge is moved in one direction, and the granule moves in the other. There is a local viscous flow about the granule, and the micelle moves toward the anode, if the granule is positive, or toward the cathode, if it is negative. This movement is called *electrophoresis*, and can be practically useful. The particles of a sol do not repel one another until they come quite close, and their micelles overlap, because of the shielding.

The *mobility* of the colloidal particle is its velocity in a unit field. Helmholtz developed a formula for the mobility, $M = \zeta\kappa/4\pi\eta$. Here, κ is the dielectric constant of the external phase, η its viscosity, and ζ is the potential difference across the micelle from the outside to the adsorbed charges on the particle, that is, through the fluid that is sliding around the granule. From measurements of M, it is possible to find ζ, which becomes a kind of "fudge factor" since it is hard to calculate. For the small gold particles in the red sol, $M = 4 \times 10^{-4}$ cm^2/s-V, and $\zeta = -0.058$ V. The negative sign indicates that the gold migrates to the anode, and so has a negative charge. The Helmholtz equation gives $M = 4.15 \times 10^{-4}$, which doesn't prove much except that we know how to use the equation. Since the equation is written in esu, we must divide by $(300)^2$ to convert volt to statvolt.

In order to create a lyophobic sol, we must either reduce a mass to colloidal size, called *dispersion*, or we must build the colloidal particles from molecules, called *condensation*. In either case, a third substance, a *peptizing* agent, may have to be added to stabilize the sol. This agent can supply ions that will be adsorbed on the particles resulting from dispersion or condensation to give them a stabilizing charge. For clays, the OH^- ion is a peptizing agent, which can be supplied by alkalis. Dispersion can be done mechanically, in a *colloid mill* that grinds the substance into small, equal particles. Another method is with an electric arc. Metal electrodes are used, at a

current of 5-10A and voltage of 30-40V. Bredig made particles of about 40 nm by this method, and it was improved by Svedburg to obtain sols of many metals down to 5 nm particle size. Ultrasonics can also be used to disperse sols.

When a sol is created in a nonpolar solvent, the particles may not be charged (and must be stabilized by some other means). They do not then exhibit electrophoresis or other electrical phenomena depending on granule charges.

Colloids and Light

A homogeneous phase or solution does not disturb the propagation of light, except to change its phase velocity to $v = c/n$, where c is the speed of light in vacuum and n is the index of refraction. In a gas, density fluctuations that are a natural result of the free movement of the molecules can scatter light. *Scattering* is the emission of light in all directions, which decreases the intensity of the ordered beam. This Rayleigh scattering is proportional to the inverse fourth power of the wavelength, so blue light is scattered more than red, giving the blue color of the clear sky. Scattering should be distinguished from *absorption*, which is the conversion of the energy of the light to other forms. Both scattering and absorption cause *attenuation* of the light beam. The transmitted beam and the scattered light may be colored if the scattering or absorption is not constant with wavelength. The blue sky and the orange sunset colors have the same cause, Rayleigh scattering by density fluctuations.

A colloidal system contains particles that affect a light beam by scattering and absorption. If the particles are of a size comparable to the wavelength of light or larger, they scatter or absorb light independently. The same thing happens if they are separated by distances comparable to or greater than the wavelength of light. The wavelength of visible light is 400-700 nm, with the maximum sensitivity at 555 nm. This is in the middle of the range of colloidal dimensions, so colloids can be expected to have significant effects on a light beam.

One common effect of colloids is *turbidity*, an effect like that of stirring up mud in water. Slight turbidity may not be noticed until a beam of light passes through the colloid. Colloidal systems need not be turbid: a gel may be quite transparent when the particles are small. Solutions, as homogeneous phases, are not turbid. The turbidity causes scattering so that the path of the light beam can be clearly seen. This is called the *Tyndall effect*, and the observed scattered light is called the *Tyndall cone*. John Tyndall (1820-1893) was Faraday's successor at the Royal Institution. He suggested that the blue sky was caused by scattering by dust particles, but Rayleigh later found the true cause, showing that the sky would be blue even if the air were pure. The scattered light is polarized perpendicularly to the direction of the beam if the particles are approximately spherical and small. If the particles are nonspherical, or larger than a wavelength, the scattered light will be partially polarized.
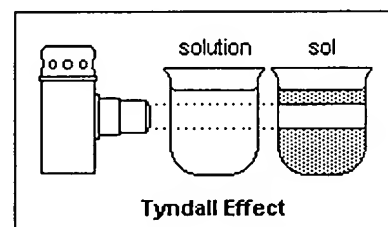
Tyndall Effect

The Tyndall effect is a common atmospheric phenomenon. Searchlights produce Tyndall cones in slightly hazy air. Smoke is often blue when seen in scattered light, orange in transmitted light. This was quite clear in the summer of 2002, when forest fires near Denver put smoke in the air, and the sunlight became a strange reddish color. The crepuscular rays seen at sunset, which seem to radiate from the position of the sun, are parallel Tyndall cones. A laser beam may make a distinct Tyndall cone in dusty air. If you have a piece of polarizing filter, try to determine the polarization of any Tyndall cones you may observe. All the Tyndall cones that you see are evidence of lyophobic sols.

If the sol is composed of transparent particles with an index of refraction considerably different from that of the external phase, and they are present in sufficient concentration, the sol wil be come opaque and white, the limit of turbidity. If the particles have the same index of refraction, the Tyndall effect will be small. This property is used in enamels, which are opaque glasses fused onto a metal substrate, and in pottery glazes. Stannic oxide, for example, gives a white enamel or glaze.

A beam of bright sunlight entering through a window may be marked with moving bright specks that are light

scattered from colloidal dust grains that are always present in the air. The grains themselves, which may be submicroscopic, are not seen, only the light they scatter. This principle is used in the *ultramicroscope* that allows individual, submicroscopic particles to be observed. Only the light from them is detected against a dark background, so that they can be counted and their motion observed; no image of the particles can be formed. The instrument consists of a bright light source, a slit and optics to focus the slit on the sample, and a microscope. A thin slice of the sample is illuminated by the slit. By turning the slit 90° the depth of the area viewed can be determined. The direction of viewing is at right angles to the illumination. Some ultramicroscopes are coaxial and use a different illumination method. If the number of particles per unit volume is found in this way, by counting using a squared graticule, and the weight of colloid per unit volume is known, then the size of the particles can be determined.

Colloids can produce color. The red of a gold sol or ruby glass has already been mentioned, where the color is due to the wavelength dependence of scattering and absorption. Color can also be produced by the interference of white light, especially if there are thin films or a periodic regularity in the density. The colors in thin oil films are familiar, and the films are, of course, colloidal in thickness. Color produced by such means is called *structural*. Color produced by absorption by colored pigments is called *pigmental*. The blue color seen in blue eyes and birds' feathers is structural, caused by scattering by fibers. Brown pigments in the iris modify the blue color to green, then overwhelm it to make brown eyes. Much color in the insect world is structural, such as the colors of a butterfly's wings, often combined with pigmental color to produce a great variety. The greenish colors of crude oil and its products are a result of colloidal suspensions.

Aerosols

An aerosol of colloidal solid particles may be called a *smoke*, while if the particles are liquid, it is a *fog*. Sometimes the two are combined, in a suspension of solid particles with an adsorbed liquid film on the surface. The original *smog* was a smoke with a liquid film of sulphuric acid, which made it excessively unpleasant to breathe. The Great Smog occurred in London on 5 December 1952, killing nearly 4000 people who had respiratory problems, and stimulating clean air legislation. Now it usually lacks the smoke, and is a fog of some unpleasant liquid coming from motorcars instead. Aerosols have the usual characteristics of lyophobic sols: a strong Brownian movement, the scattered blue light of the Tyndall effect, and stabilization with particle charges.

Clouds are aerosols of water particles, supported by the Brownian motion like any sol. The droplets are produced by condensation of water vapor on *condensation nuclei*, which are usually hygroscopic particles of dust, or positive ions. The mist above splashing water is positively charged, with compensating negative charge in the form of unhydrated negative ions. For condensation to occur, the air must be supersaturated for water vapor. The radius of the droplets is large for colloidal particles, and they are often supported by updrafts more than by Brownian motion. The radius of cirrus cloud droplets may be 2 μm. When they reach a radius of about 0.04 mm, the droplets fall as rain, often coalescing with others. The largest raindrops have a radius of about 3.6 mm, and such large drops are rare.

Raindrops can be blown upwards into freezing air by updrafts, gathering water by coalescence with others, and freezing to a solid ball. This can happen repeatedly, forming large hailstones that eventually fall. The largest hail reported may be the 3" diameter hail that fell in Bloomington, Ind. in 1917. A farmer was killed by hail near Lubbock, Texas in the 1930's, but this is the only reported fatality.

Saturated air can be expanded adiabatically to cool it and achieve supersaturation. This can be done in the laboratory with the Wilson cloud chamber with an adiabatic expansion against a piston or the equivalent, which does work that cools the air. The cooling is given by $T_2/T_1 = (V_1/V_2)^{k-1}$, where k is the ratio of the specific heat at constant pressure to the specific heat at constant volume (1.4 for air). In clean air, condensation occurs for a volume ratio greater than 1.25. From 1.25 to 1.34, the condensation falls as fine rain. For 1.25 to 1.28 the condensation is on negative ions, and the particle radius is 200μm. For 1.28 to 1.34 the condensation is on the positive ions, and the particle radius is 20μm. For larger expansion ratios, the mists can be colored: 1.408 gives green, 1.422 purple, and 1.429 red.

At the lower expansion ratios, condensation is difficult enough that it may occur along the tracks of alpha particles, which ionize strongly, making the tracks visible. The condensation soon settles out, since the droplets are large. The chamber can work with alcohol vapor as well as water vapor.

The vapor pressure p' of a small drop of radius r is greater than the vapor pressure p of a plane surface of the liquid. The vapor pressure p' is given by $\ln(p'/p) = (1/RTd)(2\gamma/r - q^2/8\pi r^4)$, if q is the charge density on the surface. γ is the surface tension of the liquid. This shows that a charge of either sign will stabilize a small droplet against evaporation. In the absence of a charge, small droplets will evaporate in favor of large drops. Electric charges may explain the stability of clouds, and the fact that rain may not fall from them.

An aerosol of starch grains, with a density of $100g/m^3$, has a very large surface area, and adsorbs O_2 from the atmosphere. Starch grains in flour are from 5 nm to 200 nm in diameter. It is no wonder that it is a violent explosive. Coal ground to pass through a 200-300 mesh sieve can be blown directly into a fire as a convenient fuel. It can also make a sol with fuel oil to form a *colloidal fuel* that can be used exactly like fuel oil. Coal dust is reputed to be a fire hazard, but it is not as dangerous as starch dust. Many "coal dust" explosions may have another cause.

Smudge pots are used to protect agricultural plants from frost. They are small fires producing dense smoke. The heat produced by the fires is probably one of the most important effects. The smoke may provide condensation nuclei for the dews of evening, increasing the heat by the latent heat of the condensed vapor. The aerosol blanket slows loss of heat by radiation, which can be very important into a clear night sky.

Smoke is also used for military purposes, for concealment or signalling. White phosphorus burns to hygroscopic P_2O_5, which forms a dense white fog in humid air. Silicon tetrachloride mixed with ammonium hydroxide gives a dense white smoke of ammonium chloride and metasilicic acid. This smoke is used in skywriting, since it is easily made from liquids when needed. The navy's smoke for concealment was made by restricting the air supply to the boilers, producing thick black smoke from the funnels. Radar and the end of gunnery has rendered smoke screens useless. Colored smoke may be used for signalling.

Emulsions

An *emulsion* is a colloidal system in which both phases are liquid. If the liquids were miscible, they would form a solution, so emulsions are lyophobic colloids. The typical example is water and oil. The internal phase is determined by which component has the higher surface tension. This component will form spherical bubbles immersed in the other, which will be a continuous phase. The granules of an emulsion may be large, even microscopic. An emulsifying agent is usually required to form a stable emulsion. The emulsifying agent, or *protective colloid*, is *surface-active*, meaning that it reduces the surface tension of the liquid, and so tends to concentrate in boundary films. In the case of water and oil, sodium oleate, a *soap* reduces the water surface tension and raises that of the oil, so that the emulsion will be oil droplets in water, and quite stable. There are many other *detergents*, but sodium oleate will serve as a good example.

Oleic acid is a fatty acid with the formula $CH_3(CH_2)_7CH=CH(CH_2)_7COOH$, a monounsaturated carboxylic acid with a long hydrocarbon chain. Fats are glyceryl esters of this acid. Glycerol has three OH groups, each of which can take the H off the end of the oleic acid and stick the rest to the glycerol framework, making a *triglyceride*. Boiling the fat with NaOH makes three molecules of sodium oleate, a liquid soap. The hydrocarbon chain nestles up to the oil, the sodium to the water, and peptizes the oil. The emulsion can be made by simply shaking oil, water and soap together, but this will not make droplets of a uniform size. The larger droplets may "cream off" in this case, and float to the surface of the emulsion. The emulsion may be *homogenized* by blowing it through small orifices under a pressure of 4000 to 5000 psi. The small, uniform drops that result will make a stable, long-lasting emulsion.

Milk is an emulsion of oil ("butterfat") in a watery sol of the hydrophilic protein casein in which the external phase is a solution of lactose and various salts. Milk will "cream" unless homogenized, since the fat globules

range from 100 nm to 22 μm in diameter. Cream can contain from 29% to 56% fat, in packed globules stabilized by casein. Human milk contains albumin in addition to casein. Mayonnaise is an emulsion of oil in water, using egg yolks as an emulsifying agent. Hollandaise sauce is another emulsion, of butter in lemon juice, again using egg yolks as an emulsifying agent. Butter itself is an emulsion, this time of water droplets in oil. The cosmetic "vanishing cream" is an oil-in-water emulsion. If this is reversed, "nourishing cream" is a water-in-oil emulsion. Crude oil as it comes from the well is often emulsified with water. In this case, heating is sufficient to "break" the emulsion, and separate the oil from the salt water. Many insecticides are oil-in-water emulsions for spraying. The oil wets the oily leaf surfaces and sticks, while the water carrying the poison evaporates. Lubricating grease is a water-in-oil emulsion. The emulsifying agent, calcium oleate, is soluble in oil, not in water, and so makes the water the internal phase. The idea here is to make the lubricant stiff, so it will not drip off.

Whether a component of an emulsion is the internal or external phase is determined by the relative surface tensions, not be the amounts of the components. Equal-sized globules can close-pack like spheres to occupy 74% of the volume. The internal phase can be even higher in concentration if the globules are not all the same size, so the smaller can huddle in the voids left by the larger. Because of the presence of an emulsifying agent, emulsions are very stable, and "breaking" them when required can be difficult.

To find out whether an emulsion is oil-in-water or water-in-oil, the effect of adding a small amount of either oil or water to a sample of the emulsion on a microscope slide is observed. If you add the external phase, it will mix easily and quickly, but the internal phase will not mix and remain a drop. This is called the *dilution test*.

Foams

A foam may be an internal phase of gas in an external phase of liquid or solid. In a liquid foam, a colloidal adsorptive agent forms a film that bounds the gas bubble. Bubbles blown with soap solution are related to foams, but are quite large and have an independent existence. Smaller bubbles in a mass form the more usual foam. People washing dishes or clothes are reassured by a thick layer of soap foam on the water, showing that there is still detergent left to emulsify additional oil. Such foams are mainly air, with very little liquid. The colloidal dimension in a foam is the thickness of the film, not the size of the bubble. The bubble is lighter than its surroundings, and will rise to the top, where it joins the foam. In beer, the foam is stabilized by albumin and by the hop resins added to the beer. When carbon dioxide is released, it uses the adsorptive agent it finds to make the foam. This "head" on Guinness stout is famous and creamy--and carefully engineered. Meringue is a dried foam using egg albumin. Marshmallows use sugared gelatin for the same purpose.

Ore flotation depends on the property of the adsorptive agent to wet the valuable metallic sulphides or other ore, but not the silicates, which are preferentially wetted by water. Note again the central role played by surface chemistry. A froth is made with water and the adsorptive agent, and mixed with the ore to be beneficiated. The froth floats to the surface, where it is skimmed off, together with the enriched ore. In a few special cases, the valuable mineral is wetted by the water, while the gangue sticks to the oil. We use the buoyancy of the bubbles to effect the separation.

A fire-fighting foam is made from mixing water, aluminium sulphate and sodium bicarbonate with an adsorptive agent. The carbon dioxide that is released makes a dry foam, while the other ingredients form a kind of gel. This foam can be used on all kinds of fires, including burning oils.

Examples of solid foams are pumice, meerschaum, and Ivory® soap. The white soap has colloidal air beaten into it so that it will float. Meerschaum, "sea foam" in German, is a light-colored metamorphic rock associated with serpentine, and is a magnesium silicate, also known as *sepiolite* from its resemblance to light cuttlefish (sepia) bone. It is soft, smooth, light and translucent, used mainly for carving smoking pipes. It is fibrous and porous, with gaseous inclusions, apparently a dried gel. It is so porous that it floats on water, in spite of its mass density of 2.0 g/cc. Pumice, an extrusive igneous rock, is a solidifed foam of volcanic glass, usually obsidian. It also floats on water, and makes a good gentle abrasive. Diatomaceous earth consists of the microscopic shells of diatoms, very common marine plants, made of opaline silica and very porous. It adsorbs nitroglycerine to make dynamite, rendering it much less sensitive and much safer to handle. Bread is, of course, a dried foam as well. The protein

gluten makes the film that surrounds the CO_2 bubbles produced by the enzyme zymase secreted by the yeast.

Zymase acts on the sugars (hexose) produced from starch by other enzymes, and also makes ethyl alcohol at the same time as the carbon dioxide. The alcohol is often the desired product! Hydrophilic gluten and water make a good gel in "strong" flours that include as much CO_2 as possible and hold the starch granules. Rye flour has little gluten, and will not make light bread by itself. Foams aid digestion by providing as large a surface area as possible.

Gels

So far we have looked at lyophobic colloids, which will have nothing to do with the other phase. A lyophilic colloid, by contrast, actively seeks out the other phase and adsorbs it strongly. In most cases, the other phase is water, so we are dealing with hydrophilic colloids. Aluminum hydroxide and orthosilicic acid are inorganic examples. Most organic colloids are hydrophilic. Gelatin is of animal origin, derived from protein, made by boiling bones and horny parts. Gums are of vegetable origin. Gums are branching polysaccharides, soluble in water. They include the *mucilages* carrageenan (from Irish moss, a seaweed) and agar-agar (also from seaweed), which are sulphate esters. Gum arabic is from the acacia tree, and gum mastic is from the *Pistacia lentiscus*. Gums are secreted by trees to protect and seal wounds. When you find any of these in a list of food ingredients, they are for the purpose of making a gel. Ice cream may contain guar gum, cellulose gum, locust bean gum and carrageenan. These gums are not digestible.

A *resin* is similar to a gum in purpose, but is insoluble in water. Resins are notably secreted by evergreens, and are terpene derivatives, soluble in turpentine and similar solvents. Rosin is the residue when turpentine is distilled. Amber and copal are other natural resins, while alkyd and phenolic resins are artificial, used in plastics and paint.

Gelatin or gums dissolve in hot water. As the clear colloidal system cools, its viscosity increases steadily. The viscosity of the external phase is not affected in hydrophobic sols, by distinction. At some point, the system *gels*, forming a wobbly but definitely solid body. This is really an extraordinary thing to happen. If you heat the gel, it will melt and form a viscous liquid. On cooling, it will gel again. If you dry it out, it will shrink and look horrible. On adding water, it will plump up again into a wiggly gel. These colloids are called *reversible* or *elastic*. The gels formed from inorganic hydroxides will not reform a gel once they have dried out, and the dry form will be brittle. The pore spaces will still be there, however, and will absorb moisture and other substances. Silica gel is a widely used substance. Though it can be renewed by heating and live to absorb again, it will never again be wobbly and gelatinous. I say absorb, since it will appear to be this, but on a microscopic scale it is still adsorption, of course.

Gels are used as culture media for microorganisms. Gelatin was originally used, but it melts at 37°C, and so cannot be used to study microorganisms at body temperature. Agar-agar makes a gel that can stand higher temperatures, so it is used in preference as a culture medium, poured into the familiar Petri dish. It was first used by Robert Koch.

The colloidal phase in a gelatin is fibrillar, composed of fibers of colloidal cross-section. When a gel sets, these fibers form a tangled mass like a pile of brush, that holds the system together. Droplets in a gel are lens-shaped, showing the packing. There has been quite a bit of controversy over the structure of gels, but the fibrillar structure seems correct. The original idea of a cellular structure is untenable. The fibers adsorb large quantities of water, and there are also droplets of water, so that the gel is mainly water, given a doubtful rigidity by the stacks of fibers.

Pectin is a gelatin-like protein substance found in the rind of citrus fruit, in apples and generally in fruits. If a slightly acid solution of pectin is made 65% or 70% sucrose, it will gel. This is the reaction used to make jams. The verb *pectize* is used to describe the creation of a gel, as peptize is to create a sol.

Gels have some curious properties. As they age, *syneresis* may occur, which is the loss of liquid. This is a result of the closer agglomeration of the colloid. The reduced active area requires less water, so the excess water is eliminated. It does not mean that the gel is deteriorating. Another property is *thixotropy*. On agitation, the gel

becomes fluid, but reverts to the gel when left alone. Fresh gelatin gels are quite thixotropic, and advantage can be taken of this to add ingredients to a jelly. The "thixo-" comes from the future of the Greek verb for "touch," *thixomai*, and a thixotropic substance would be one whose state changes with touching.

Colloids and Membranes

Let's review the phenomenon of *osmosis*. In the diagram, we have put some solution into a container closed off by a *semipermeable membrane,* and put the container into a vessel containing the pure solvent. Consider the dots as representing the dissolved substance. This applies to a sol, as well as to a solution, but there will be more "solute" particles in the solution. The membrane can be cellophane, but ordinary wrapping cellophane cannot be used, since it has been lacquered to close the pores. The pores must be small enough to prevent the solute from passing through. The solvent is found to cross the membrane and enter the solution, making it more dilute. The level of the solution rises to some height h in equilibrium. If d is the density, then π = dgh is the *osmotic pressure*. This is the pressure required on the solution side to make the rate of movement of the solvent the same in both directions across the membrane. If the solution is dilute, van't Hoff's equation gives the osmotic pressure: $\pi V = nRT$, where the volume V of the solution contains n moles of solute.

Osmosis
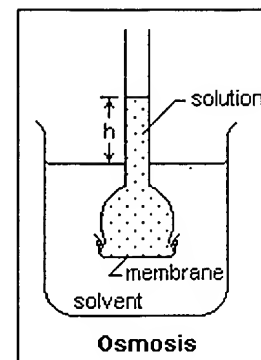
The osmotic pressure of a solution containing 1 mole of solute per 1 kg of solvent, called a 1 molal solution, is quite large, about 25 atmospheres (as we can estimate from van't Hoff's equation). Not only is this hard on cellophane membranes, but would require a liquid column 825 feet high, which is inconvenient. Nevertheless, osmotic pressures are high enough to push fluids to the tops of high trees (this is actually a complex subject about which there is controversy). Strong semipermeable membranes can be made by precipitating insoluble salts in the pores of unglazed porcelain. Sols will exert quite modest osmotic pressures, since there are many fewer particles per unit volume. In fact, the pressures are so low that they cannot be used in most cases to find the number of particles per unit volume. However, the molecular weight of haemoglobin was determined in this way. Cell walls are semipermeable membranes. If an erythrocyte (red blood cell) is put into pure water, it will swell and burst because it contains a solution of electrolytes in a semipermeable membrane. If put into strong salt solution, it will become dehydrated and shrivel. Solutions of the same osmotic pressure are called *isotonic.* Isotonic solutions are used to prevent damage to biological systems. Erythrocytes are about 8.6 μm in diameter and 2.6 μm thick, and slightly concave on the faces. They are a bit large for colloidal particles, though the blood plasma is a colloid that can gel under certain circumstances. Like platelets, which are definitely colloidal, they are not living cells like the leucocytes that accompany them.

The separation of colloids and crystalloids is called *dialysis*, and can be carried out with a suitable semipermeable membrane, just as in osmosis. Chemists actually distingush dialysis, in which the components diffuse at different rates across a membrane, from *ultrafiltration*, in which larger particles are mechanically stopped while smaller ones are allowed to pass. Ultrafiltration can occur through gels, while dialysis uses dialytic membranes. There is no fundamental difference between the processes, however.

Dialysis is carried out in the body by the kidneys, which separate the crystalloids urea, uric acid, hippuric acid and ammonia compounds from the colloidal albumin and other proteins of the blood. The crystalloids diffuse more rapidly across the interface than the larger particles. In the laboratory, we can put the sample to be dialyzed into a container like that used for osmosis, and change the solvent as it becomes concentrated in the crystalloids. Parchment paper can be used for the dialytic membrane. A bag of parchment paper can be filled with the sample to be dialyzed, and it can be suspended in a bath of moving warm water for rapid dialysis. Membranes can also be prepared from other animal membranes, or collodion (nitrocellulose dissolved in alcohol and ether), or artificial sheet polymers. Electrodialysis can also be used, taking advantage of ion migration in an electric field.

Dialysis has many industrial applications. Sugar is extracted from sugar beets by using the cell walls as dialytic membranes, washing cut beets in warm water. Dialysis is used in the artificial fiber industry to separate alkali from the colloidal fiber material, and in the pharmaceutical industry for the purification of colloidal medicines.

Dialysis is used in artificial kidney machines to simulate the action of the kidneys.

Colloids and Adsorbents

As has been pointed out, absorption is a volume effect, while adsorption is a surface effect. Colloids, having large surface areas for a given volume, are excellent at adsorption. A cubic centimeter of charcoal can have a surface area of 1000 m^2, so a little charcoal can do a lot of adsorbing. Adsorption may be specific. For example, Ni, Pt and Pd in colloidal form adsorb H_2 up to 1000 or 3000 times their volume. Palladium is the best at this. At red heat, palladium metal will absorb hydrogen readily, and release it at even higher temperature. Black palladium powder can be made by reducing $PdCl_2$ in solution. Because of the adsorption, these metals, in colloidal form, make excellent catalysts for hydrogenation.

Usually, adsorption is not very specific, and a wide variety of substances can be adsorbed on a certain medium. Adsorption is temperature-sensitive, being much more effective at low temperatures, and evolving the adsorbed substances at higher temperatures. Carbon at room temperature does not adsorb oxygen and nitrogen, but does so at liquid-nitrogen temperatures. Adsorption is generally accompanied by a negative change in enthalpy, so it is *exothermic*. The temperature dependence is a consequence of LeChatelier's Principle.

The three most commonly used adsorbents are carbon as charcoal, alumina and silica. When specially prepared as adsorbents, they are called *activated*. Activation is usually a matter mainly of heating, and perhaps some chemical cleaning. A saturated adsorbent may be re-activated by heating, say at 175°C for 6-8 hours in air. Charcoal may be prepared from wood, bone, blood and sugar. The charcoal from different sources has different impurities and therefore somewhat different characteristics. Charcoal is a *nonpolar* adsorbent that is good for organic vapors and nonpolar substances in general. Alumina and Silica are *polar* adsorbents and are best for polar substances, like water.

Charcoal is used in gas masks, since it readily adsorbs toxic organic vapors rather indiscriminately. It does not adsorb carbon monoxide or ammonia well, so specal adsorbents for these must be included. Carbon monoxide is usually oxidized to the dioxide, and ammonia by silica gel. Therefore, a complete gas mask canister contains a mechanical filter, charcoal, silica gel, and an oxidant for CO. Charcoal can be used to produce ultra-high vacuum by cooling it to liquid nitrogen temperatures. If charcoal in a stout glass tube in a U-shape is saturated with chlorine or sulphur dioxide, and then sealed off, the gas is liquefied when the charcoal end of the tube is heated, and the other end is cooled. Natural gas may be filtered through charcoal to remove higher alkanes. Pentane and hexane are more strongly adsorbed than the lighter methane and ethane. Charcoal is, in general, used when organic substances are to be removed from a gas.

Alumina gel and silica gel are produced by drying the gel produced by precipitating the hydroxides in water. Alumina gel is good for water vapor, carbon dioxide and alcohol. It makes an excellent laboratory dessicant. A small amount of colorimetric indicator is added that is blue when the alumina is dry, but turns pink when it has adsorbed water and is alkaline. The dessicant can then be regenerated by heating in an oven. Alumina gel is generally used for drying organic liquids, which it also decolorizes, and for removing acids from oils. It also removes oil vapor from compressed air. Alumina gel is a good example of the nonspecifity of adsorption.

Silica gel is the most generally useful adsorbent. It is especially good at adsorbing benzene, for example from coke-oven gas. Silica gel is used to dry carbon dioxide, hydrogen and oxygen before they are liquefied or solidified. It is often found in small bags in sealed packages that must be protected from humidity. These bags are easily re-activated by heating. Silica gel can be used to dry natural gas for pipeline transport, to prevent the formation of ice clathrates at low temperatures. These clathrates can form above the freezing point and easily clog pipelines.

Other colloidal adsorbents found naturally are *diatomite*, also known as diatomaceous earth or kieselguhr, which is composed of diatom shells made from opaline silica, and *bentonite*, a strongly hydrophilic colloidal clay consisting mainly of montmorillonite. Bentonite can clarify and deodorize petroleum, purify and soften water,

make drilling mud, plug leaks as a grout, improve cleaning powders, and destroy building foundations by swelling. Diatomite has perhaps even more uses than bentonite. Both are valuable colloidal minerals.

Adsorbents are imporant in dyeing fabrics. Often the fabric will not adsorb the dye directly, since the dye may be polar and the fiber nonpolar. However, gels like amphoteric metal hydroxides, especially aluminium hydroxide, may cling to the fibers while strongly adsorbing the dyes. Such intermediates are called *mordants*, which are usually colloids. The dye and the mordant together, without the fiber, is called a *lake* (from the same word that gave "lacquer"). Purple of Cassius is a famous lake, formed on stannic hydroxide gel by colloidal gold.

References

Most textbooks of Elementary Chemistry will include a chapter on colloids that makes a good introduction to the subject.

R. J. Hartman, *Colloid Chemistry* (London: Pitman & Sons, 1949). A classic reference with a great deal of description of colloid phenomena of all types.

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Granulation

Malcolm Summers, Michael Aulton

CHAPTER CONTENTS

INTRODUCTION TO GRANULATION

Granulation is the process in which **primary powder particles** are made to adhere to form larger, multiparticle entities called **granules**. Pharmaceutical granules typically have a size range between 0.2 and 4.0 mm, depending on their subsequent use. In the majority of cases this will be in the production of tablets or capsules, when granules will be made as an intermediate product and have a typical size range between 0.2 and 0.5 mm, but larger granules are used as a dosage form in their own right (see Chapter 24).

Granulation normally commences after initial dry mixing of the necessary powdered ingredients so that a uniform distribution of each ingredient through the mix is achieved. After granulation the granules will either be packed (when used as a dosage form), or they may be mixed with other excipients prior to tablet compaction or capsule filling.

Reasons for granulation

The reasons why granulation is often necessary are as follows.

To prevent segregation of the constituents of the powder mix

Segregation (or demixing, see Chapter 13) is due primarily to differences in the size or density of the components of the mix, the smaller and/or denser particles concentrating at the base of a container with the larger and/or less dense ones above them. An ideal granulation will contain all the constituents of the mix in the correct proportion in each granule, and segregation of the ingredients will not occur (Fig. 25.1).

It is also important to control the particle size distribution of the granules because, although the individual components may not segregate, if there is a wide size distribution the granules themselves may segregate. If this occurs in the hoppers of sachet-filling machines, capsule-filling machines or tablet machines, products with large weight variations will result. This is because these machines fill by volume rather than weight, and if different regions in the hopper contain granules of different sizes (and hence bulk density), a given volume in each region will contain a different weight of granules. This will lead to an unacceptable distribution of the drug content within the batch of finished product, even though the drug is evenly distributed, weight per weight, through the granules.
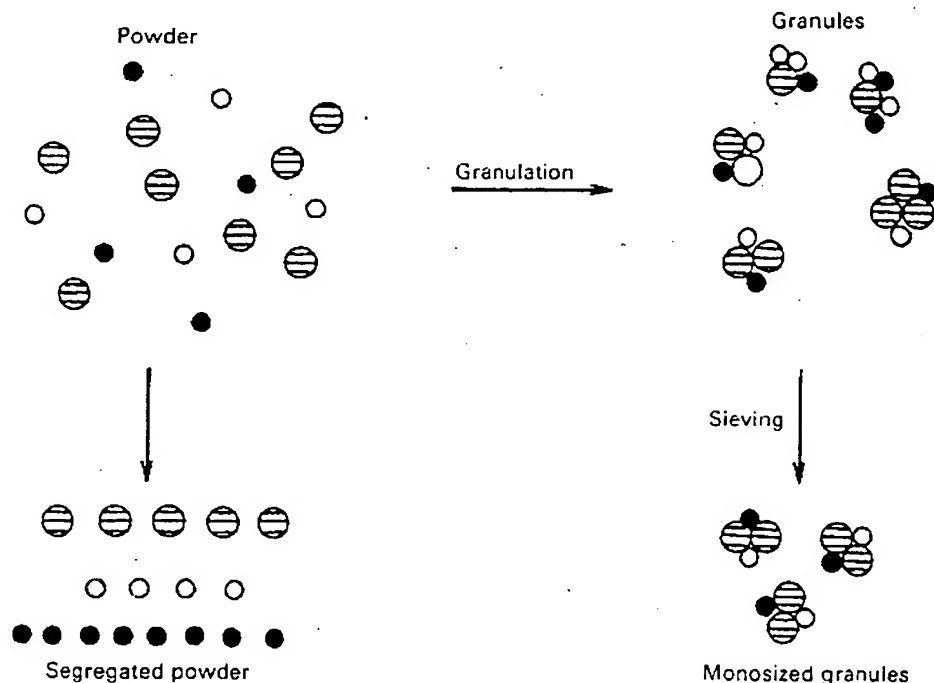

Fig. 25.1   Granulation to prevent powder segregation.

To improve the flow properties of the mix

Many powders, because of their small size, irregular shape or surface characteristics, are cohesive and do not flow well. Poor flow will often result in a wide weight variation within the final product owing to variable fill of tablet dies etc. Granules produced from such a cohesive system will be larger and more isodiametric, both factors contributing to improved flow properties.

To improve the compaction characteristics of the mix

Some powders are difficult to compact even if a readily compactable adhesive is included in the mix, but granules of the same formulation are often more easily compacted and produce stronger tablets. This is associated with the distribution of the adhesive within the granule and is a function of the method employed to produce the granule. Often solute migration (see Chapter 26) occurring during the postgranulation drying stage results in a binder-rich outer layer to the granules. This in turn leads to direct binder–binder bonding, which assists the consolidation of weakly bonding materials.

Other reasons

The above are the primary reasons for the granulation of pharmaceutical products, but there are other reasons that may necessitate the granulation of powdered material:

1. The granulation of toxic materials will reduce the hazard associated with the generation of toxic dust that may arise when handling powders. Suitable precautions must be taken to ensure that such dust is not a hazard during the granulation process. Thus granules should be non-friable and have a suitable mechanical strength.
2. Materials which are slightly hygroscopic may adhere and form a cake if stored as a powder. Granulation may reduce this hazard, as the granules will be able to absorb some moisture and yet retain their flowability because of their size.
3. Granules, being denser than the parent powder mix, occupy less volume per unit weight. They are therefore more convenient for storage or shipment.

Methods of granulation

Granulation methods can be divided into two types: **wet** methods, which use a liquid in the process, and **dry** methods in which no liquid is used.

In a suitable formulation a number of different excipients will be needed in addition to the drug. The common types used are diluents, to produce a unit dose weight of suitable size, and disintegrating agents, which are added to aid the break-up of the granule when it reaches a liquid medium, e.g. on ingestion by the patient. Adhesives in the form of a dry powder may also be added, particularly if dry granulation is employed. These ingredients will be mixed before granulation.

Dry granulation

In the dry methods of granulation the primary powder particles are aggregated under high pressure. There are two main processes. Either a large tablet (known as a '*slug*') is produced in a heavy-duty tabletting press (a process known as '*slugging*') or the powder is squeezed between two rollers to produce a sheet of material ('*roller compaction*'). In both cases these intermediate products are broken using a suitable milling technique to produce granular material, which is usually sieved to separate the desired size fraction. The unused fine material may be reworked to avoid waste. This dry method may be used for drugs that do not compress well after wet granulation, or those which are sensitive to moisture.

Wet granulation (involving wet massing)

Wet granulation involves the massing of a mix of dry *primary powder particles* using a *granulating fluid*. The fluid contains a solvent which must be volatile so that it can be removed by drying, and be non-toxic. Typical liquids include water, ethanol and isopropanol, either alone or in combination. The granulation liquid may be used alone or, more usually, as a solvent containing a dissolved *adhesive* (also referred to as a *binder* or *binding agent*) which is used to ensure particle adhesion once the granule is dry.

Water is commonly used for economical and ecological reasons. Its disadvantages as a solvent are that it may adversely affect drug stability, causing hydrolysis of susceptible products, and it needs a longer drying time than do organic solvents. This increases the length of the process and again may affect stability because of the extended exposure to heat. The primary advantage of water is that it is non-flammable, which means that expensive safety precautions such as the use of flameproof equipment need not be taken. Organic solvents are used when

water-sensitive drugs are processed, as an alternative to dry granulation, or when a rapid drying time is required.

In the traditional wet granulation method the wet mass is forced through a sieve to produce wet granules which are then dried. A subsequent screening stage breaks agglomerates of granules and removes the fine material, which can than be recycled. Variations of this traditional method depend on the equipment used, but the general principle of initial particle aggregation using a liquid remains in all of the processes.

Effect of granulation method on granule structure

The type and capacity of granulating mixers significantly influences the work input and time necessary to produce a cohesive mass, adequate liquid distribution and intragranular porosity of the granular mass. The method and conditions of granulation affect intergranular and intragranular pore structure by changing the degree of packing within the granules. It has been shown that precompressed granules, consisting of compressed drug and binder particles, are held together by simple bonding during compaction. Granules prepared by wet massing consist of intact drug particles held together in a sponge-like matrix of binder. Fluidized-bed granules are similar to those prepared by the wet massing process, but possess greater porosity and the granule surface is covered by a film of binding agent. With spray-dried systems the granules consist of spherical particles composed of an outer shell and an inner core of particles. Thus the properties of the granule are influenced by the manufacturing process.

GRANULATION MECHANISMS

Particle-bonding mechanisms

To form granules, bonds must be formed between powder particles so that they adhere and these bonds must be sufficiently strong to prevent breakdown of the granule to powder in subsequent handling operations.

There are five primary bonding mechanisms between particles:

1. Adhesion and cohesion forces in the immobile liquid films between individual primary powder particles;
2. Interfacial forces in mobile liquid films within the granules;
3. The formation of solid bridges after solvent evaporation;
4. Attractive forces between solid particles;
5. Mechanical interlocking.

Different types of mechanism were identified in each group and the ones discussed below are those that are relevant to pharmaceutical granulations.

Adhesion and cohesion forces in immobile films

If sufficient liquid is present in a powder to form a very thin, immobile layer, there will be an effective decrease in interparticulate distance and an increase in contact area between the particles. The bond strength between the particles will be increased because of this, as the van der Waals forces of attraction are proportional to the particle diameter and inversely proportional to the square of the distance of separation.

This situation will arise with adsorbed moisture and accounts for the cohesion of slightly damp powders. Although such films may be present as residual liquid after granules prepared by wet granulation have been dried, it is unlikely that they contribute significantly to the final granule strength. In dry granulation, however, the pressures used will increase the contact area between the adsorption layers and decrease the interparticulate distance, and this will contribute to the final granule strength.

Thin, immobile layers may also be formed by highly viscous solutions of adhesives, and so the bond strength will be greater than that produced by the mobile films discussed below. The use of starch mucilage in pharmaceutical granulations may produce this type of film.

Interfacial forces in mobile liquid films

During wet granulation liquid is added to the powder mix and will be distributed as films around and between the particles. Sufficient liquid is usually added to exceed that necessary for an immobile layer and to produce a mobile film. There are three states of water distribution between particles, which are illustrated in Figure 25.2.

At low moisture levels, termed the *pendular state*, the particles are held together by lens-shaped rings of liquid. These cause adhesion because of the surface tension forces of the liquid/air interface and the hydrostatic suction pressure in the liquid bridge. When all the air has been displaced from between
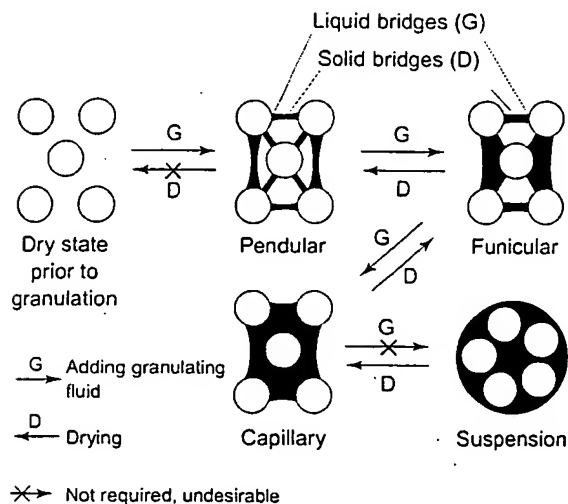
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Fig. 25.2 Water distribution between particles of a granule during formation and drying.

the particles the *capillary state* is reached, and the particles are held by capillary suction at the liquid/air interface, which is now only at the granule surface. The *funicular state* represents an intermediate stage between the pendular and capillary states. Moist granule tensile strength increases about three times between the pendular and the capillary state.

· It may appear that the state of the powder bed is dependent upon the total moisture content of the wetted powders, but the capillary state may also be reached by decreasing the separation of the particles. In the massing process during wet granulation, continued kneading/mixing of material originally in the pendular state will densify the wet mass, decreasing the pore volume occupied by air and eventually producing the funicular or capillary state without further liquid addition.

In addition to these three states, a further state, the droplet, is illustrated in Figure 25.2. This will be important in the process of granulation by spray-drying of a suspension. In this state, the strength of the droplet is dependent upon the surface tension of the liquid used.

These wet bridges are only temporary structures in wet granulation because the moist granules will be dried. They are, however, a prerequisite for the formation of solid bridges formed by adhesives present in the liquid, or by materials that dissolve in the granulating liquid.

Solid bridges

These can be formed by:

1. partial melting
2. hardening binders
3. crystallization of dissolved substances.

Partial melting Although not considered to be a predominant mechanism in pharmaceutical materials, it is possible that the pressures used in dry granulation methods may cause melting of low melting-point materials where the particles touch and high pressures are developed. When the pressure is relieved, crystallization will take place and bind the particles together.

Hardening binders This is the common mechanism in pharmaceutical wet granulations when an adhesive is included in the granulating solvent. The liquid will form liquid bridges, as discussed above, and the adhesive will harden or crystallize on drying to form solid bridges to bind the particles. Adhesives such as polyvinylpyrrolidone, the cellulose derivatives (such as carboxymethylcellulose) and pregelatinized starch function in this way.

Crystallization of dissolved substances The solvent used to mass the powder during wet granulation may partially dissolve one of the powdered ingredients. When the granules are dried, crystallization of this material will take place and the dissolved substance then acts as a hardening binder. Any material soluble in the granulating liquid will function in this manner, e.g. lactose incorporated into dry powders granulated with water.

The size of the crystals produced in the bridge will be influenced by the rate of drying of the granules: the slower the drying time, the larger the particle size. It is therefore important that the drug does not dissolve in the granulating liquid and recrystallize, because it may adversely affect the dissolution rate of the drug if crystals larger than that of the starting material are produced.

Attractive forces between solid particles

In the absence of liquids and solid bridges formed by binding agents, there are two types of attractive force that can operate between particles in pharmaceutical systems.

Electrostatic forces may be important in causing powder cohesion and the initial formation of agglomerates, e.g. during mixing. In general they do not contribute significantly to the final strength of the granule.

Van der Waals forces, however, are about four orders of magnitude greater than electrostatic forces and contribute significantly to the strength of granules produced by dry granulation. The magnitude of these forces will increase as the distance between

adjacent surfaces decreases, and in dry granulation this is achieved by using pressure to force the particles together.

Mechanisms of granule formation

In the dry methods, particle adhesion takes place because of applied pressure. A compact or sheet is produced which is larger than the granule size required, and therefore the required size can be attained by milling and sieving.

In wet granulation methods, liquid added to dry powders has to be distributed through the powder by the mechanical agitation created in the granulator. The particles adhere to each other because of liquid films, and further agitation and/or liquid addition causes more particles to adhere. The precise mechanism by which a dry powder is transformed into a bed of granules varies for each type of granulation equipment, but the mechanism discussed below serves as a useful broad generalization of the process.

The proposed granulation mechanism can be divided into three stages.

Nucleation

Granulation starts with particle–particle contact and adhesion due to liquid bridges. A number of particles will join to form the pendular state illustrated in Figure 25.2. Further agitation densifies the pendular bodies to form the capillary state, and these bodies act as nuclei for further granule growth.

Transition

Nuclei can grow in two possible ways: either single particles can be added to the nuclei by pendular bridges, or two or more nuclei may combine. The combined nuclei will be reshaped by the agitation of the bed.

This stage is characterized by the presence of a large number of small granules with a fairly wide size distribution. Providing that this distribution is not excessively large, this is a suitable end-point for granules used in capsule and tablet manufacture, as relatively small granules will produce a uniform tablet die or capsule fill. Larger granules may give rise to problems in small-diameter dies owing to bridging across the die and uneven fill.

Ball growth

Further granule growth produces large, spherical granules and the mean particle size of the granulating system will increase with time. If agitation is con-

tinued, granule coalescence will continue and produce an unusable, overmassed system, although this is dependent upon the amount of liquid added and the properties of the material being granulated.

Although ball growth produces granules that may be too large for pharmaceutical purposes, some degree of ball growth will occur in planetary mixers and it is an essential feature of some spheronizing equipment.

The four possible mechanisms of ball growth are illustrated in Figure 25.3.

Coalescence Two or more granules join to form a larger granule.

Breakage Granules break into fragments which adhere to other granules, forming a layer of material over the surviving granule.

Abrasion transfer Agitation of the granule bed leads to the attrition of material from granules. This abraded material adheres to other granules, increasing their size.

Layering When a second batch of powder mix is added to a bed of granules the powder will adhere to the granules, forming a layer over the surface and increasing the granule size. This mechanism is only relevant to the production of layered granules using spheronizing equipment.

There will be some degree of overlap between these stages and it will be very difficult to identify a given stage by inspection of the granulating system. For end-product uniformity it is desirable to finish every batch of a formulation at the same stage, and this may be a major problem in pharmaceutical production.

Using the slower processes, such as the planetary mixer, there is usually sufficient time to stop the process before overmassing occurs. With faster granulation equipment the duration of granulation can only be used as a control parameter when the formulation is such that granule growth is slow and takes place at a fairly uniform rate. In many cases, however, the transition from a non-granulated to an overmassed system is very rapid, and monitoring equipment is necessary to stop the granulation at a predetermined point, known as granulation end-point control.

PHARMACEUTICAL GRANULATION EQUIPMENT

Wet granulators

There are three main types of granulator used in the pharmaceutical industry for wet granulation.
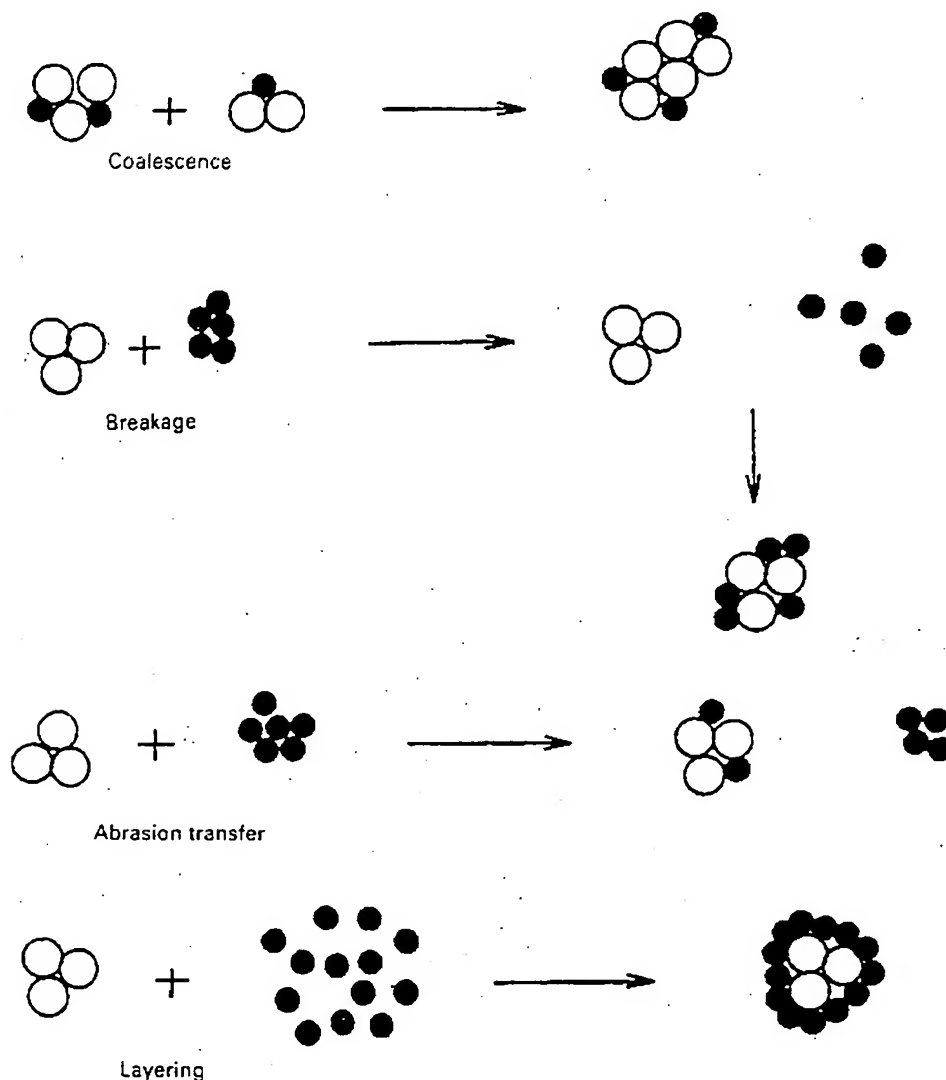
Fig. 25.3 Mechanisms of ball growth during granulation.

Shear granulators

In the traditional granulation process a planetary mixer is often used for wet massing of the powders, e.g. Hobart, Collette, Beken (Fig. 25.4). Powder mixing usually has to be performed as a separate operation using suitable mixing equipment. With some formulations, such as those containing two or three ingredients in approximately equal quantities, however, it may be possible to achieve a suitable mix in the planetary mixer without a separate stage.

The mixed powders are fed into the bowl of the planetary mixer and granulating liquid is added as the paddle of the mixer agitates the powders. The planetary action of the blade when mixing is similar to that of a household mixer.

The moist mass has then to be transferred to a granulator, such as an oscillating granulator (Fig. 25.5). The rotor bars of the granulator oscillate and force the moist mass through the sieve screen, the size of which determines the granule size. The mass should be sufficiently moist to form discrete granules when sieved. If excess liquid is added, strings of material will be formed and if the mix is too dry the mass will be sieved to powder and granules will not be formed.

The granules can be collected on trays and transferred to a drying oven, although tray drying suffers from three major disadvantages:
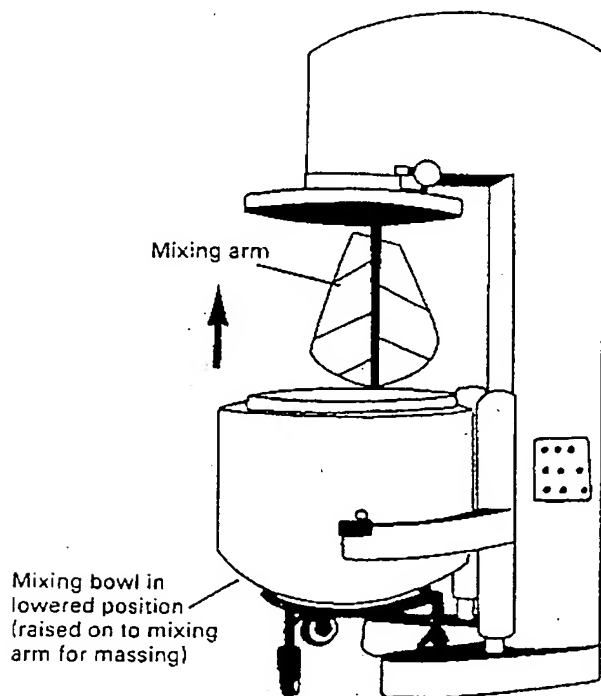
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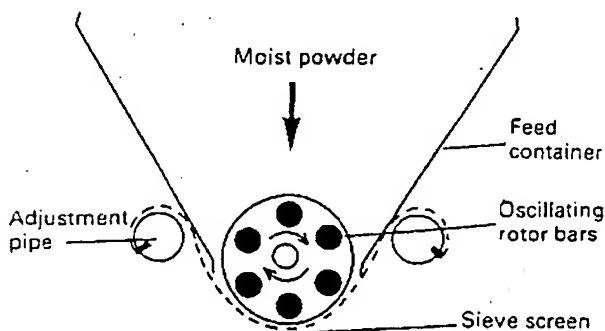Fig. 25.4   Planetary mixer for wet massing.

Fig. 25.5   Oscillating granulator.

1. The drying time is long..
2. Dissolved material can migrate to the upper surface of the bed of granules, as the solvent is only removed from the upper surface of the bed on the tray.
3. Granules may aggregate owing to bridge formation at the points of contact of the granules.

To deaggregate the granules and remix them, a sieving stage is necessary after drying.

An alternative method is to dry the granules using a fluidized-bed drier. This is quicker and, as it keeps the individual granules separated during drying, it reduces the problems of aggregation and intergranular solute migration, thereby reducing the need for a sieving stage after drying.

The disadvantages of this traditional granulation process are its long duration, the need for several pieces of equipment, and the high material losses that can be incurred because of the transfer stages. Advantages are that the process is not very sensitive to changes in the characteristics of the granule ingredients (e.g. surface area variations in different batches of an excipient), and the end-point of the massing process can often be determined by inspection.

High-speed mixer/granulators

This type of granulator (e.g. Diosna, Fielder) is used extensively in pharmaceutics. The machines have a stainless steel mixing bowl containing a three-bladed main impeller, which revolves in the horizontal plane, and a three-bladed auxiliary chopper (breaker blade) which revolves either in the vertical or the horizontal plane (Fig. 25.6).

The unmixed dry powders are placed in the bowl and mixed by the rotating impeller for a few minutes. Granulating liquid is then added via a port in the lid of the granulator while the impeller is turning. The granulating fluid is mixed into the powders by the impeller. The chopper is usually switched on when the moist mass is formed, as its function is to break up the wet mass to produce a bed of granular material. Once a satisfactory granule has been produced, the granular product is discharged, passing through a wire mesh which breaks up any large aggregates, into the bowl of a fluidized-bed drier.

The advantage of the process is that mixing, massing and granulation are all performed within a few minutes in the same piece of equipment. The process needs to be controlled with care as the granulation progresses so rapidly that a usable granule can be transformed very quickly into an unusable, overmassed system. Thus it is often necessary to use a suitable monitoring system to indicate the end of the granulation process, i.e. when a granule of the desired properties has been attained. The process is also sensitive to variations in raw materials, but this may be minimized by using a suitable end-point monitor.

A variation of the Diosna/Fielder type of design is the Collette–Gral mixer (Fig. 25.7). This is based on the bowl and overhead drive of the planetary mixer, but the single paddle is replaced by two mixing shafts. One of these carries three blades, which rotate in the horizontal plane at the base of the bowl, and the
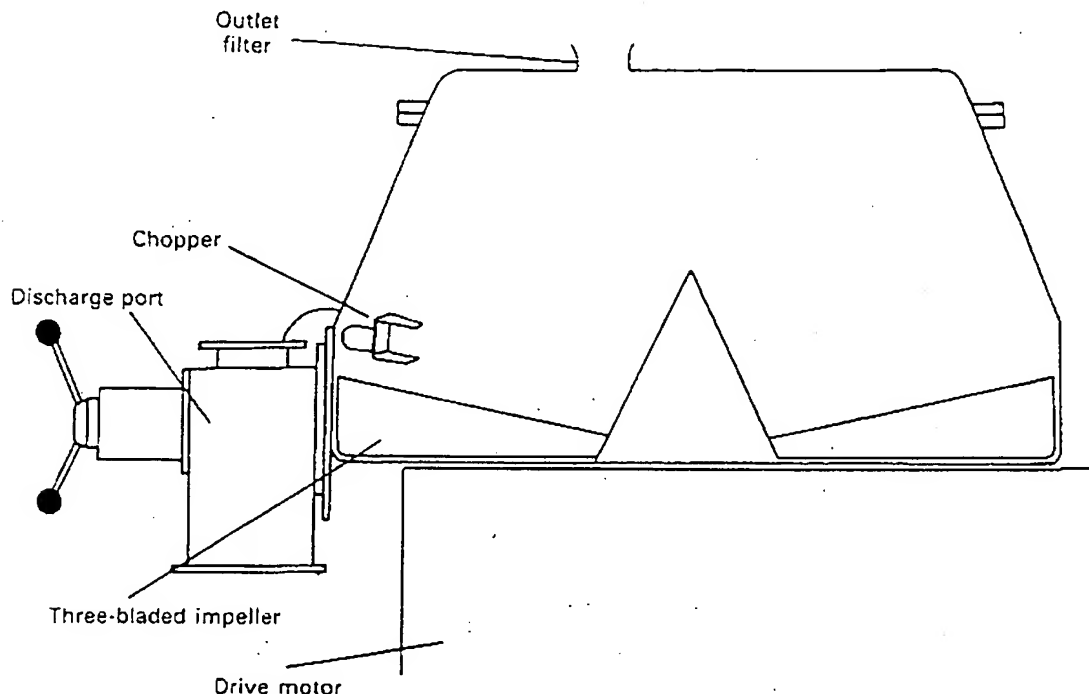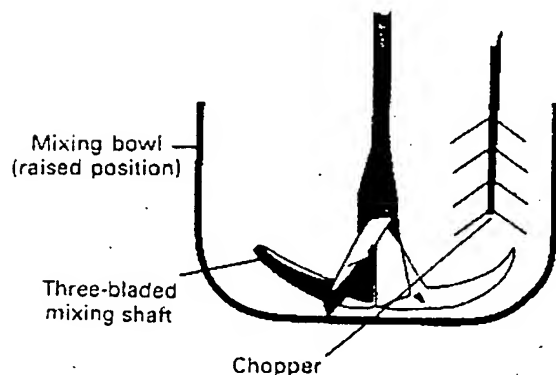
Fig. 25.6 High-speed mixer/granulator.

Fig. 25.7 Collette–Gral granulator: mixing shafts and bowl.

second carries smaller blades which act as the chopper and rotate in the horizontal plane in the upper regions of the granulating mass. Thus the operation principle is similar.

Fluidized-bed granulators

Fluidized-bed granulators (e.g. Aeromatic, Glatt) have a similar design and operation to fluidized-bed driers, i.e. the powder particles are fluidized in a stream of air, but in addition granulation fluid is sprayed from a nozzle on to the bed of powders (Fig. 25.8).

Heated and filtered air is blown or sucked through the bed of unmixed powders to fluidize the particles and mix the powders; fluidization is actually a very efficient mixing process. Granulating fluid is pumped from a reservoir through a spray nozzle positioned over the bed of particles. The fluid causes the primary powder particles to adhere when the droplets and powders collide. Escape of material from the granulation chamber is prevented by exhaust filters, which are periodically agitated to reintroduce the collected material into the fluidized bed. Sufficient liquid is sprayed to produce granules of the required size, at which point the spray is turned off but the fluidizing air continued. The wet granules are then dried in the heated fluidizing airstream.

Advantages of fluidized-bed granulation Fluidized-bed granulation has many advantages over conventional wet massing. All the granulation processes, which require separate equipment in the conventional method, are performed in one unit, saving labour costs, transfer losses and time. Another advantage is that the process can be automated once the conditions affecting the granulation have been optimized.
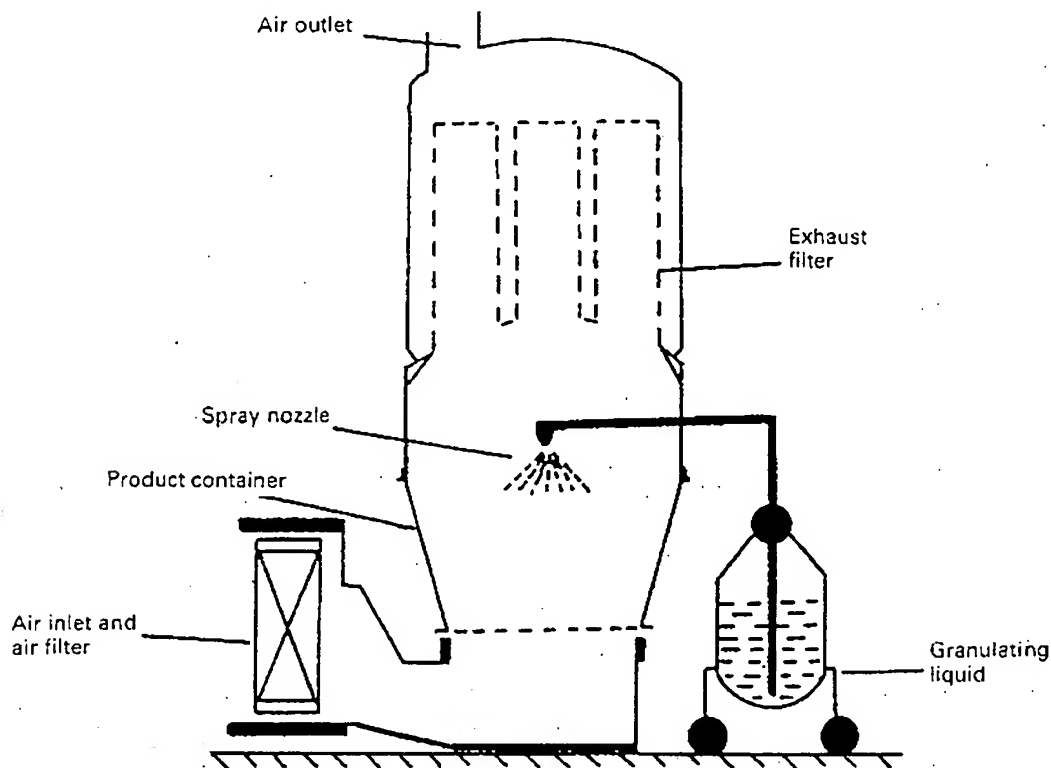
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Fig. 25.8 Fluidized-bed granulator.

Disadvantages of fluidized-bed granulation On the downside, the equipment is initially expensive and optimization of process (and product) parameters affecting granulation needs extensive development work, not only during initial formulation work but also during scale-up from development to production. Similar development work for the traditional process and that using high-speed granulators is not as extensive.

This long and very product-specific development process has proved to be a serious problem with fluidized-bed granulation in the pharmaceutical industry. There are numerous apparatus, process and product parameters that affect the quality of the final granule. These are listed in Table 25.1. The extent of this list, coupled with the fact that each formulation presents its own individual development problems,

Table 25.1 Apparatus, process and product variables influencing fluidized-bed granulation

Apparatus parameters	Process parameters	Product parameters
Air distribution plate	Bed load	Type of binder
Shape of granulator body	Fluidizing air flow rate	Quantity of binder
Nozzle height	Fluidizing air temperature	Binder solvent
Positive or negative pressure operation	Fluidizing air humidity	Concentration of granulating solution
Scale-up	Atomization	Temperature of granulation solution
	Nozzle type	
	Spray angle	Starting Materials
	Spraying regime	Fluidization
	Liquid flow rate	Powder hydrophobicity
	Atomizing air flow rate	
	Atomizing air pressure	
	Droplet size	

has led to fluidized-bed granulation not reaching its full potential in pharmaceutical production. This is exacerbated by the reality that most pharmaceutical companies have a wide range of products made at relatively small batch sizes, unlike other industries (fertilizers, herbicides, foodstuffs) where fluidized-bed granulation is used successfully and extensively.

Spray-driers

These differ from the method discussed above in that a dry, granular product is made from a solution or a suspension rather than initially dry primary powder particles. The solution or suspension may be of drug alone, a single excipient or a complete formulation.

The process of spray-drying is discussed fully in Chapter 26. The resultant granules are free-flowing hollow spheres and the distribution of the binder in such granules (at the periphery following solute migration during drying) results in good compaction properties.

This process can be used to make tablet granules, although it is probably economically justified for this purpose only when suitable granules cannot be produced by the other methods. Spray-drying can convert hard elastic materials into more ductile ones. Spray-dried lactose is the classic example, and its advantages over α-lactose monohydrate crystals when compacted are discussed in Chapter 27.

The primary advantages of the process are the short drying time and the minimal exposure of the product to heat owing to the short residence time in the drying chamber. This means that little deterioration of heat-sensitive materials takes place, and it may be the only process suitable for this type of product.

Spheronizers/pelletizers

For some applications it may be desirable to have a dense, spherical pellet of the type difficult to produce with the equipment above. Such pellets are used for controlled drug release products following coating with a suitable polymer coat and filling into hard gelatin capsules. Capsule filling with a mixture of coated and non-coated drug-containing pellets would give some degree of programmed drug release after the capsule shell dissolves.

A commonly used process involves the separate processes of wet massing, followed by extrusion of this wet mass into rod-shaped granules and subsequent spheronization of these granules. Because this process is used so frequently to produce modified-release multiparticulates, it will be discussed in some detail.

Extrusion/spheronization

Extrusion/spheronization is a multistep process used to make uniformly sized spherical particles. It is used primarily to produce multiparticulates for controlled drug release applications. The major advantage over other methods of producing drug-loaded spheres or pellets is the ability to incorporate high levels of active ingredients without producing excessively large particles (i.e. minimal excipients are necessary).

The main steps of the process are:

1. *Dry mixing of ingredients* to achieve a homogenous powder dispersion;
2. *Wet massing* to produce a sufficiently plastic wet mass;
3. *Extrusion* to form rod-shaped particles of uniform diameter;
4. *Spheronization* to round off these rods into spherical particles;
5. *Drying* to achieve the desired final moisture content;
6. *Screening* (optional) to achieve the desired narrow size distribution.

Applications of extrusion/spheronization

Potential applications are many, but relate mainly to controlled drug release and improved processing.

Controlled drug release Both immediate-release and controlled-release pellets can be formed. In turn, these pellets can either be filled into hard gelatin capsule shells or compacted into tablets to form unit dosage forms. Pellets can contain two or more ingredients in the same individual unit, or incompatible ingredients can be manufactured in separate pellets.

Pellets can be coated in sub-batches to give, say, rapid-, intermediate- and slow-release pellets in the same capsule shell. Dense multiparticulates disperse evenly within the GI tract and have less variable gastric emptying and intestinal transit times than do single units, such as coated monolithic tablets.

Processing The process of extrusion/spheronization can be used to increase the bulk density, improve flow properties and reduce the problems of dust usually encountered with low-density, finely divided active and excipient powders.

Extrusion/spheronization is a more labour-intensive process than other forms of granulation and should therefore only be considered when other methods are either not satisfactory for that particular formulation or are inappropriate (i.e. when spheres are required).

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Desirable properties of pellets

Uncoated pellets:

- Uniform spherical shape
- Uniform size
- Good flow properties
- Reproducible packing (into hard gelatin capsules)
- High strength
- Low friability
- Low dust
- Smooth surface
- Ease of coating.

Once coated:

- Maintain all of the above properties
- Have desired drug-release characteristics.

The process

Dry mixing of ingredients This uses normal powder-mixing equipment.

Wet massing This stage also employs normal equipment and processes as used in wet granulation. There are two major differences in the granulation step compared with granulation for compaction:

1. The amount of granulation fluid
2. The importance of achieving a uniform dispersion of fluid.

The amount of fluid needed to achieve spheres of uniform size and sphericity is likely to be greater than that for a similar tablet granulation. Poor liquid dispersion will produce a poor-quality product.

Extrusion Extrusion produces rod-shaped particles of uniform diameter from the wet mass. The wet mass is forced through dies and shaped into small cylindrical particles with uniform diameter. The extrudate particles break at similar lengths under their own weight. Thus the extrudate must have enough plasticity to deform, but not so much that the extruded particles adhere to other particles when collected or rolled in the spheronizer.

There are many designs of extruder, but generally they can be divided into three classes, based on their feed mechanism:

- Screw-feed extruders (axial or end-plate, dome and radial)
- Gravity-feed extruders (cylinder roll, gear roll, radial)
- Piston-feed extruders (ram).

The first two categories (Fig. 25.9) are used for both development and production, but the latter is only

Screw-feed extruders

axial   radial

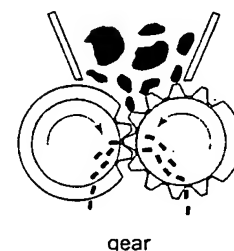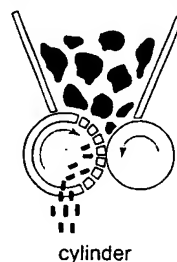Gravity-feed extruders

cylinder   gear
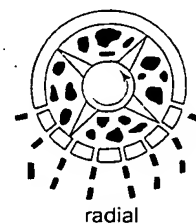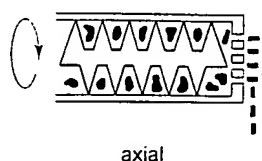
Fig. 25.9 Schematic representation of production extruders.

used for experimental development work as it is easy to add instrumentation.

The primary extrusion process variables are:

- the feed rate of the wet mass
- the diameter of the die
- the length of the die
- the water content of the wet mass.

The properties of the extrudate, and hence the resulting spheres, are very dependent on the plasticity and cohesiveness of the wet mass. In general, an extrudable wet mass needs to be wetter than that appropriate for conventional granulation by wet massing.

Spheronization The function of the fourth step in the process (i.e. spheronization) is to round off the rods produced by extrusion into spherical particles.

This is carried out in a relatively simple piece of apparatus (Fig. 25.10). The working part consists of a bowl with fixed side walls and a rapidly rotating bottom plate or disc. The rounding of the extrudate into spheres is dependent on frictional forces generated by particle–particle and particle–equipment collisions. The bottom disc has a grooved surface to increase these forces. Two geometric patterns are generally used:

- A cross-hatched pattern with grooves running at right-angles to one another
- A radial pattern with grooves running radially from the centre of the disc.
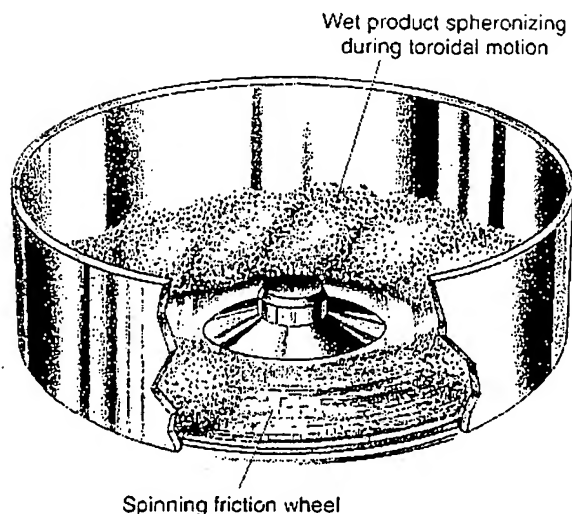
Fig. 25.10 A spheronizer showing the characteristic toroidal (rope-like) movement of the forming pellets in the spheronizer bowl during operation.
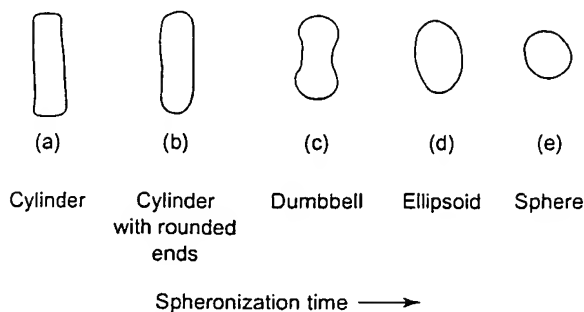

Spheronization time ⟶

Fig. 25.11 Representation of a mechanism of spheronization. The diagram shows a transition from cylindrical particles (a) into cylindrical particles with rounded edges (b), then dumbbells (c), to ellipsoids (d) and finally spheres (e).

The transition from rods to spheres during spheronization occurs in various stages. These are best described by examining the following diagrams (Fig. 25.11).

If the mass is too dry spheres will not be formed: the rods will only transform as far as dumbbells.

Drying A drying stage is required in order to achieve the desired moisture content. This is often the final step in the process. The pellets can be dried in any drier that can be used for conventional wet granulations, including tray dryers and fluidized-bed driers. Both are used successfully for extrusion/ spheronization. If solute migration (Chapter 26) occurs during drying of the wet spheres, this may result in:

• an increased initial rate of dissolution
• stronger pellets
• modified surfaces which might reduce the adhesion of any added film coats.

Screening Screening may be necessary to achieve the desired narrow size distribution. Normal sieves are used. If all the previous stages are performed efficiently and with careful development of process and formulation conditions, this step may not be necessary.

Formulation variables

The composition of the wet mass is critical in determining the properties of the particles produced. During the granulation step a wet mass is produced

which must be plastic, deform when extruded, and break off to form uniformly sized cylindrical particles which are easily deformed into spherical particles. Thus the process has a complex set of requirements that are strongly influenced by the ingredients of the pellet formulation.

Summary

Extrusion/spheronization is a versatile process capable of producing spherical granules with very useful properties. Because it is more labour-intensive than more common wet massing techniques its use should be limited to those applications where a sphere is required and other granulation techniques are unsuitable.

The most common application of the process is to produce spherical pellets for controlled drug release.

Care must be taken to understand the required properties of the pellets and the manner in which the process and formulation influence the ability to achieve these aims.

Rotor granulation

This process allows the direct manufacture of spheres from dry powder. In the Freund granulator, the powder mix is added to the bowl and wetted with granulating liquid from a spray (Fig. 25.12). The baseplate rotates at high speed and centrifugal force keeps the moist mass at the edges of the rotor. Here, the velocity difference between the rotor and the static walls, combined with the upward flow of air around the rotor plate, causes the mass to move in a toroidal motion, resulting in the formation of discrete spherical pellets. These spheres (actually, of course, wet granules) are dried by the heated inlet air
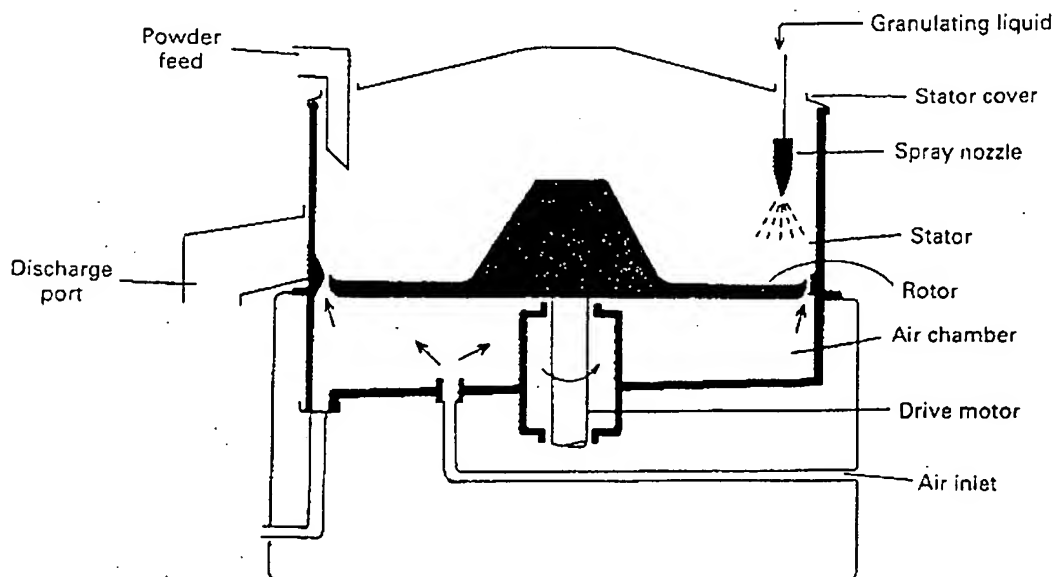
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Fig. 25.12 Freund granulator.

from the air chamber, which also acts as a positive-pressure seal during granulation.

Using this technique it is possible to continue the process and coat the pellets by subsequently spraying coating solution on to the rotating dried pellets. In addition, layered pellets can be produced by using uncoated pellets as nuclei in a second granulation with a powder mix of a second ingredient or ingredients.
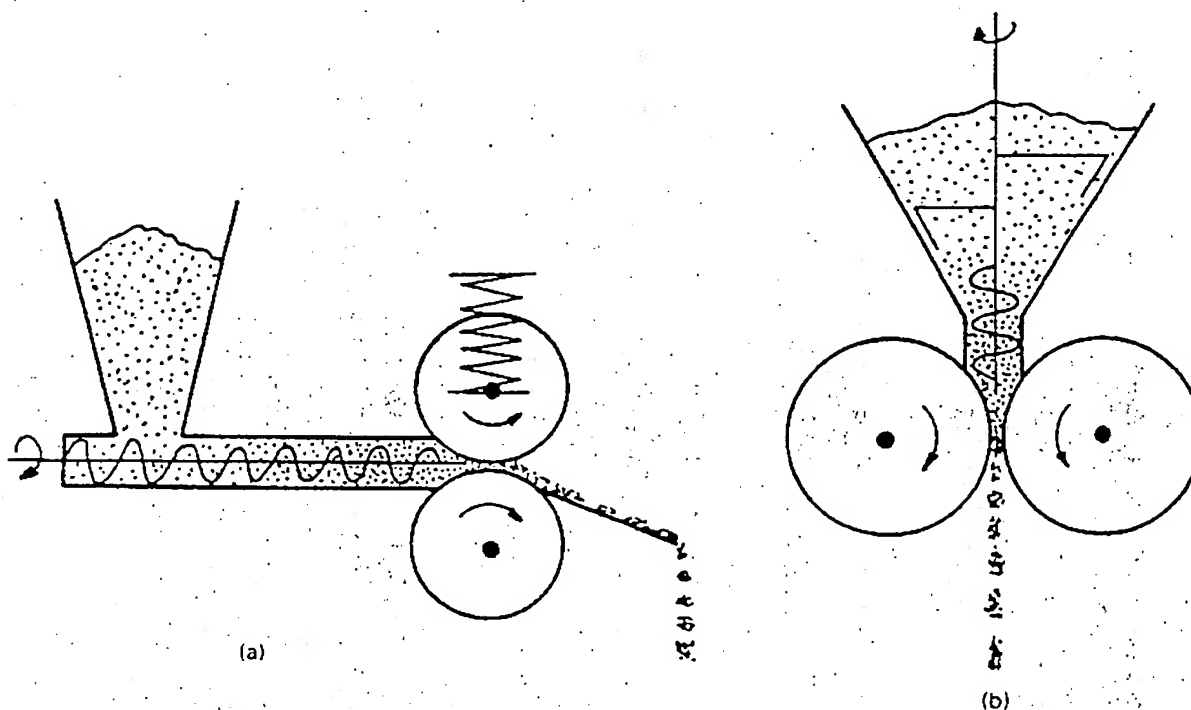

(a)

(b)

Fig. 25.13 Roller compaction: (a) Alexanderwerk and (b) Hutt types.

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Dry granulators

Dry granulation converts primary powder particles into granules using the application of pressure without the intermediate use of a liquid. It therefore avoids heat–temperature combinations that might cause degradation of the product.

Two pieces of equipment are necessary for dry granulation: first, a machine for compressing the dry powders into compacts or flakes, and secondly a mill for breaking up these intermediate products into granules.

Sluggers

The dry powders can be compressed using a conventional tablet machine or, more usually, a large heavy-duty rotary press can be used. This process is often known as 'slugging', the compact made in the process (typically 25 mm diameter by about 10–15 mm thick) being termed a 'slug'. A hammer mill is suitable for breaking the compacts.

Roller compactors

Roller compaction is an alternative gentler method, the powder mix being squeezed between two rollers to form a compressed sheet (Fig. 25.13). The sheet normally is weak and brittle and breaks immediately into flakes. These flakes need gentler treatment to break them into granules, and this can usually be achieved by screening alone.

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